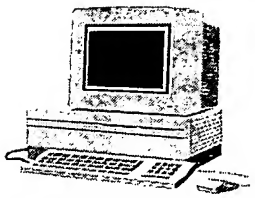
BioTech-Chem Library
Search Results
Feedback Form (Optional)



Scientific & Technical Information Center

The search results generated for your recent request are attached. If you have any questions or comments (compliments or complaints) about the scope or the results of the search, please contact ***the BioTech-Chem searcher*** who conducted the search ***or contact***:

Mary Hale, Supervisor, 308-4258
CM-1 Room 1E01

Voluntary Results Feedback Form

- *I am an examiner in Workgroup:* *(Example: 1610)*
- *Relevant prior art **found**, search results used as follows:*
  - ☐ 102 rejection
  - ☐ 103 rejection
  - ☐ Cited as being of interest.
  - ☐ Helped examiner better understand the invention.
  - ☐ Helped examiner better understand the state of the art in their technology.

  Types of relevant prior art found:
  - ☐ Foreign Patent(s)
  - ☐ Non-Patent Literature
    (journal articles, conference proceedings, new product announcements etc.)
- *Relevant prior art **not found**:*
  - ☐ Results verified the lack of relevant prior art (helped determine patentability).
  - ☐ Search results were not useful in determining patentability or understanding the invention.

Other Comments:

Drop off completed forms at the **Circulation Desk CM-1,** or send to Mary Hale, **CM1-1E01 or e-mail mary.hale@uspto.gov.**

Jan Delaval
Reference Librarian
Biotechnology & Chemical Library
CM1 1E07 – 703-308-4498
jan.delaval@uspto.gov

=> fil hcaplus
FILE 'HCAPLUS' ENTERED AT 09:53:57 ON 05 MAR 2003

FILE COVERS 1907 - 5 Mar 2003 VOL 138 ISS 10
FILE LAST UPDATED: 4 Mar 2003 (20030304/ED)

This file contains CAS Registry Numbers for easy and accurate
substance identification.

=> d all hitstr tot l59

L59 ANSWER 1 OF 8 HCAPLUS COPYRIGHT 2003 ACS
AN 2003:5786 HCAPLUS
DN 138:49952
TI Use of **sodium channel blockers** and aspirin
in manufacturing drugs for producing analgesia synergistically in mammals
IN **Ku, Baoshan; Shum, Hay Kong**
PA Wex Medical Instrumentation Co., Ltd., Peop. Rep. China
SO PCT Int. Appl., 11 pp.
CODEN: PIXXD2
DT Patent
LA Chinese
IC ICM A61K031-517
ICS A61K031-616; A61P025-04; A61P029-00
CC 1-11 (Pharmacology)
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2003000268	A1	20030103	WO 2002-CN428	20020618
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	CN 1393223	A	20030129	CN 2001-115990	20010622
PRAI	CN 2001-115990	A	20010622		

AB The present invention relates to the use of combinations of **sodium channel blocking** compds. and aspirin in manufg. drugs for producing synergistically analgesic effect in mammals, in which said compds. bind to .alpha.-subunit of SS1 or SS2 sites in the **sodium channel**. According to the invention, pharmaceutical compns. have enhancing analgesic effect, and therefore dosage of aspirin as well as its side effects would be reduced.
ST **sodium channel blocker** aspirin synergistic

interaction analgesic

IT **Ion channel blockers**
(**sodium**; use of **sodium channel blockers** and aspirin in manufg. drugs for producing analgesia synergistically in mammals)

IT Drug interactions
(synergistic; use of **sodium channel blockers** and aspirin in manufg. drugs for producing analgesia synergistically in mammals)

IT Analgesia
Analgesics
(use of **sodium channel blockers** and aspirin in manufg. drugs for producing analgesia synergistically in mammals)

IT **Sodium channel**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(.alpha.-subunit of SS1 or SS2; use of **sodium channel blockers** and aspirin in manufg. drugs for producing analgesia synergistically in mammals)

IT 7440-23-5, **Sodium**, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(transport; use of **sodium channel blockers** and aspirin in manufg. drugs for producing analgesia synergistically in mammals)

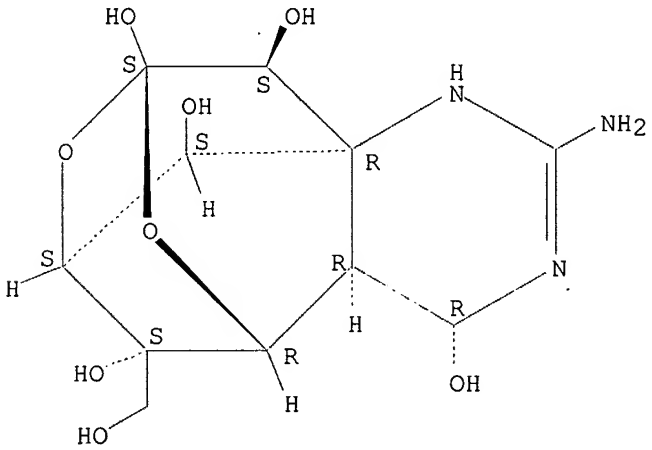
IT 50-78-2, Aspirin **4368-28-9**, TTX
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(use of **sodium channel blockers** and aspirin in manufg. drugs for producing analgesia synergistically in mammals)

IT **4368-28-9**, TTX
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(use of **sodium channel blockers** and aspirin in manufg. drugs for producing analgesia synergistically in mammals)

RN 4368-28-9 HCAPLUS

CN 5,9:7,10a-Dimethano-10aH-[1,3]dioxocino[6,5-d]pyrimidine-4,7,10,11,12-pentol, octahydro-12-(hydroxymethyl)-2-imino-, (4R,4aR,5R,7S,9S,10S,10aR,11S,12S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L59 ANSWER 2 OF 8 HCAPLUS COPYRIGHT 2003 ACS

AN 2002:905867 HCAPLUS
DN 137:363099
TI Analgesic **composition** and method
IN **Ku, Baoshan; Shum, Frank Hay Kong**
PA Wex Medical Instrumentation Co., Ltd., Peop. Rep. China
SO PCT Int. Appl., 35 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM A61K031-517
ICS A61K031-485; A61P025-04
CC 1-11 (Pharmacology)
Section cross-reference(s): 63
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2002094272	A1	20021128	WO 2002-CN339	20020520
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CN 1386505	A	20021225	CN 2001-118098	20010518
US 2002198226	A1	20021226	US 2002-62483	20020205
PRAI CN 2001-118098	A	20010518		

AB A pharmaceutical analgesic **compn. comprising** an **opioid** analgesic agent and a compd. that binds to the **SS1** or **SS2** subunit of a **sodium channel**, such as **tetrodotoxin** and **saxitoxin**, and analogs thereof. Administration of an **opioid** analgesic agent and a compd. that binds to the **SS1** or **SS2** subunit of a **sodium channel**, such as **tetrodotoxin** and **saxitoxin**, and their analogs, produces analgesia in the treatment of pain in mammals. For example, the **synergistic** analgesia effect produced by co-administering **tetrodotoxin** (TTX) and **morphine** was obsd. in a formalin test in rats. **Morphine** used alone at 0.30 mg/kg only produced 10.2% inhibition of formalin-induced pain. **Combination** of TTX at 0.19 .mu.g/kg with **morphine** at 2.50 mg/kg **increased** the inhibition rate to 86.7% from 34.9% where the latter was used alone. TTX at a dose of 0.39 .mu.g/kg (1/50 of LD50) produced an inhibition rate of 32.9% when used alone and 66.2% in **combination** with 0.15 mg/kg of **morphine**, whereas the latter only produced an inhibition rate of 7.2% when used alone.

ST **opioid sodium channel blocker** injection **synergistic** analgesic

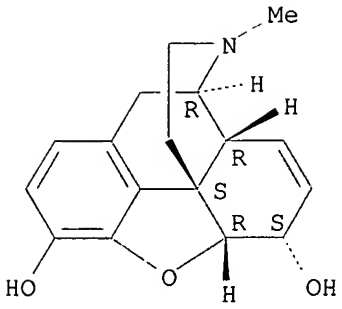
IT **Sodium channel**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(**SS1** or **SS2** subunit; **synergistic** analgesic activity of **combination** of **opioid** and **sodium channel blocker**)

IT Drug delivery systems
(injections, i.m.; **synergistic** analgesic activity of **combination** of **opioid** and **sodium channel blocker**)

IT Drug delivery systems
(injections, intrathecal; **synergistic** analgesic activity of **combination** of **opioid** and **sodium channel blocker**)

IT **Ion channel blockers**
(**sodium; synergistic** analgesic activity of **combination** of **opioid** and **sodium channel blocker**)
IT Analgesics
(**synergistic** analgesic activity of **combination** of **opioid** and **sodium channel blocker**)
IT **Opioids**
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**synergistic** analgesic activity of **combination** of **opioid** and **sodium channel blocker**)
IT Drug interactions
(**synergistic; synergistic** analgesic activity of **combination** of **opioid** and **sodium channel blocker**)
IT **52-26-6, Morphine** hydrochloride **57-27-2, Morphine**, biological studies **76-57-3, Codeine 76-99-3, Methadone 437-38-7, Fentanyl 3270-35-7, Tetrodonic acid 4368-28-9, Tetrodotoxin 7724-38-1, Tetrodaminotoxin 7724-39-2, Methoxytetrodotoxin 7724-40-5, Ethoxytetrodotoxin 7724-41-6, Deoxytetrodotoxin 13072-89-4, Anhydrotetrodotoxin 35523-89-8, Saxitoxin**
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**synergistic** analgesic activity of **combination** of **opioid** and **sodium channel blocker**)
RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE
(1) Anon; US 4022899 1977 HCAPLUS
(2) Anon; CN 1145225 A 1997 HCAPLUS
(3) Xur, Y; JIANGSU CLINICAL MEDICAL JOURNAL 2001, V5(5), P361
IT **52-26-6, Morphine** hydrochloride **57-27-2, Morphine**, biological studies **76-57-3, Codeine 76-99-3, Methadone 437-38-7, Fentanyl 3270-35-7, Tetrodonic acid 4368-28-9, Tetrodotoxin 7724-38-1, Tetrodaminotoxin 7724-39-2, Methoxytetrodotoxin 7724-40-5, Ethoxytetrodotoxin 7724-41-6, Deoxytetrodotoxin 13072-89-4, Anhydrotetrodotoxin 35523-89-8, Saxitoxin**
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**synergistic** analgesic activity of **combination** of **opioid** and **sodium channel blocker**)
RN 52-26-6 HCAPLUS
CN Morphinan-3,6-diol, 7,8-didehydro-4,5-epoxy-17-methyl-, (5.alpha.,6.alpha.)-, hydrochloride (9CI) (CA INDEX NAME)

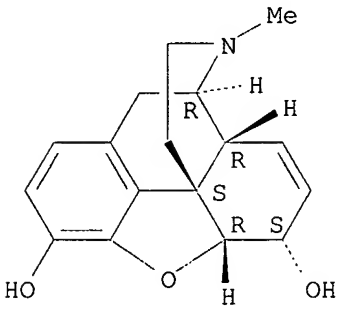
Absolute stereochemistry. Rotation (-).



● HCl

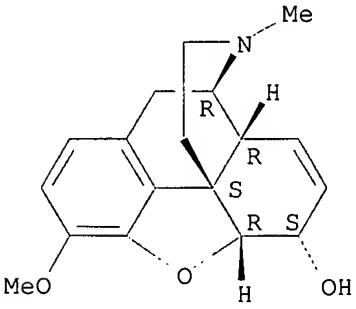
RN 57-27-2 HCAPLUS
CN Morphinan-3,6-diol, 7,8-didehydro-4,5-epoxy-17-methyl-
(5.alpha.,6.alpha.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

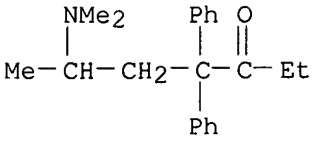


RN 76-57-3 HCAPLUS
CN Morphinan-6-ol, 7,8-didehydro-4,5-epoxy-3-methoxy-17-methyl-,
(5.alpha.,6.alpha.)- (9CI) (CA INDEX NAME)

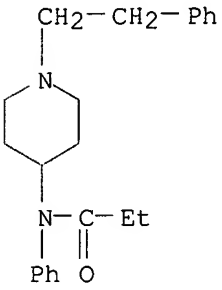
Absolute stereochemistry.



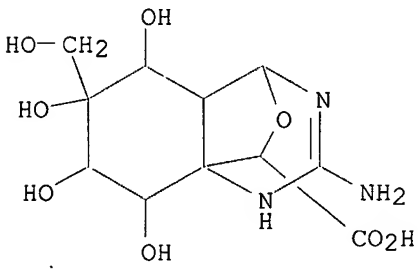
RN 76-99-3 HCAPLUS
CN 3-Heptanone, 6-(dimethylamino)-4,4-diphenyl- (7CI, 8CI, 9CI) (CA INDEX
NAME)



RN 437-38-7 HCAPLUS
CN Propanamide, N-phenyl-N-[1-(2-phenylethyl)-4-piperidinyl]- (9CI) (CA INDEX NAME)

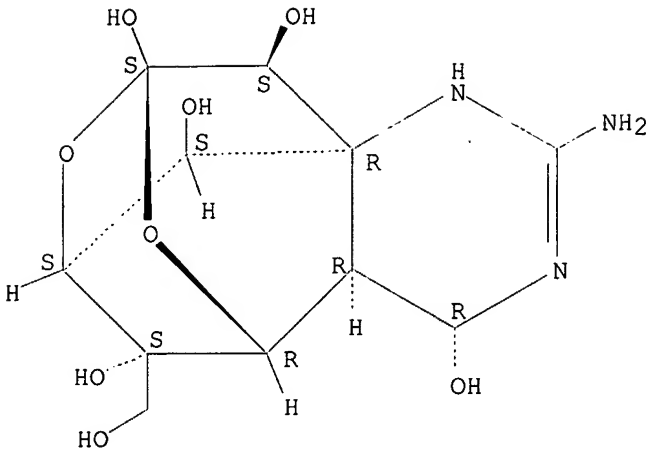


RN 3270-35-7 HCAPLUS
CN 1H-4,8a-(Epoxymethano)quinazoline-9-carboxylic acid, 2-amino-4,4a,5,6,7,8-hexahydro-5,6,7,8-tetrahydroxy-6-(hydroxymethyl)-, (4S,4aR,5R,6S,7R,8R,8aR,9R)- (9CI) (CA INDEX NAME)



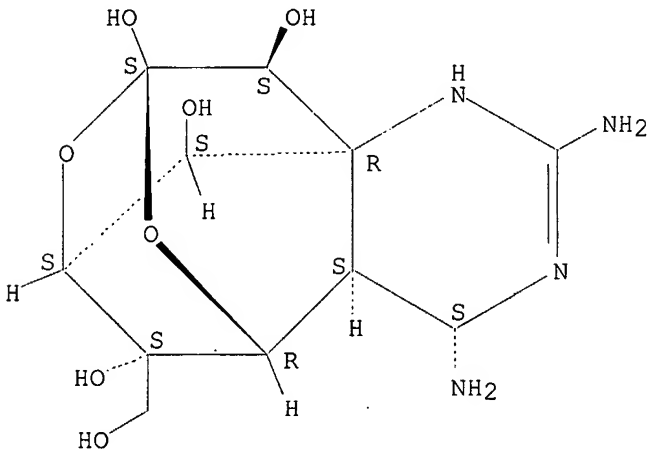
RN 4368-28-9 HCAPLUS
CN 5,9:7,10a-Dimethano-10aH-[1,3]dioxocino[6,5-d]pyrimidine-4,7,10,11,12-pentol, octahydro-12-(hydroxymethyl)-2-imino-, (4R,4aR,5R,7S,9S,10S,10aR,11S,12S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



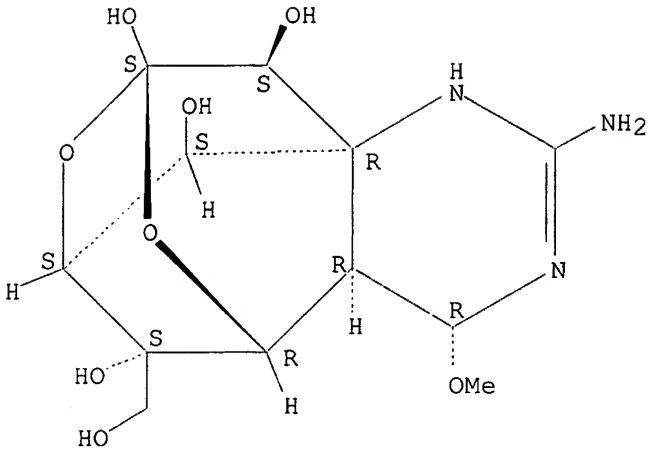
RN 7724-38-1 HCAPLUS
CN 5,9:7,10a-Dimethano-10aH-[1,3]dioxocino[6,5-d]pyrimidine-7,10,11,12-tetrol, 4-aminooctahydro-12-(hydroxymethyl)-2-imino-, (4R,4aR,5R,7S,9S,10S,10aR,11S,12S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



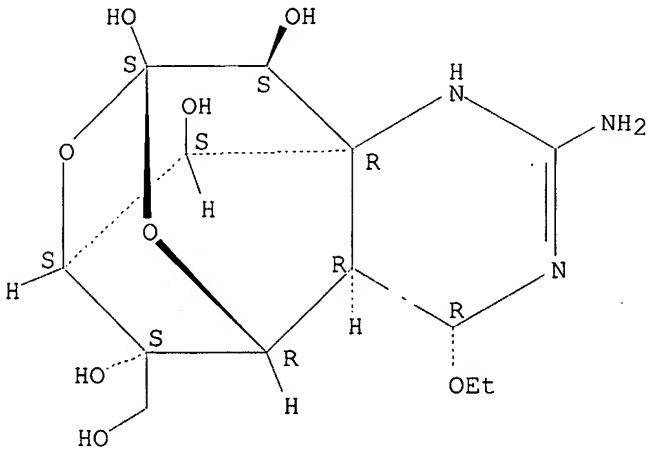
RN 7724-39-2 HCAPLUS
CN 5,9:7,10a-Dimethano-10aH-[1,3]dioxocino[6,5-d]pyrimidine-7,10,11,12-tetrol, octahydro-12-(hydroxymethyl)-2-imino-4-methoxy-, (4R,4aR,5R,7S,9S,10S,10aR,11S,12S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



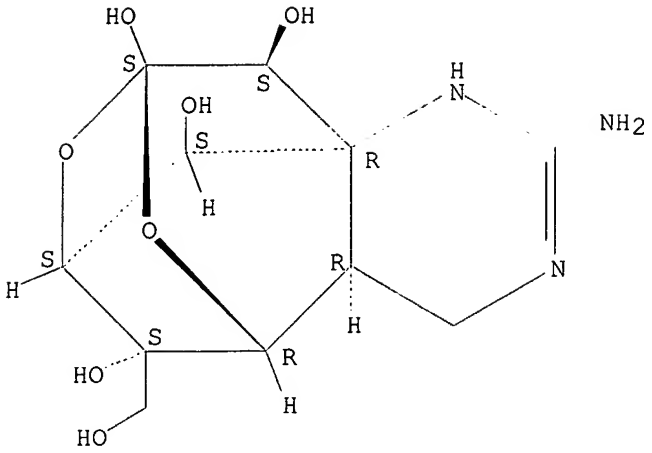
RN 7724-40-5 HCAPLUS
CN 5,9:7,10a-Dimethano-10aH-[1,3]dioxocino[6,5-d]pyrimidine-7,10,11,12-tetrol, 4-ethoxyoctahydro-12-(hydroxymethyl)-2-imino-, (4R,4aR,5R,7S,9S,10S,10aR,11S,12S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



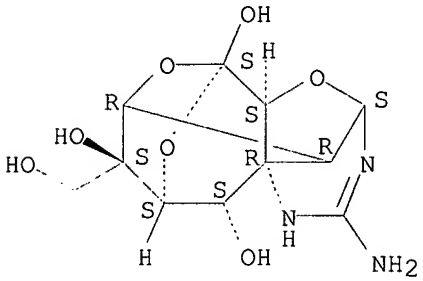
RN 7724-41-6 HCAPLUS
CN 5,9:7,10a-Dimethano-10aH-[1,3]dioxocino[6,5-d]pyrimidine-7,10,11,12-tetrol, 2-amino-1,4,4a,5,9,10-hexahydro-12-(hydroxymethyl)-, (4aR,5R,7S,9S,10S,10aR,11S,12S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



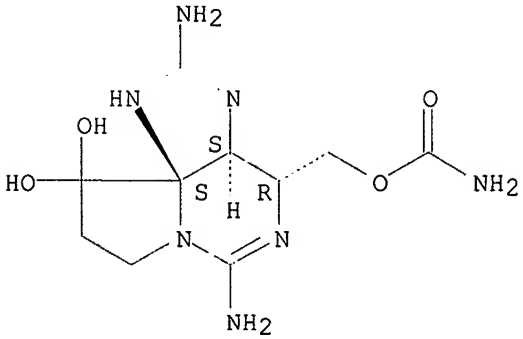
RN 13072-89-4 HCAPLUS
CN 6,10-Epoxy-4,8,11a-metheno-11aH-oxocino[4,3-f][1,3,5]oxadiazepine-6,9,11-triol, 2-amino-1,4,5a,6,8,9,10,11-octahydro-9-(hydroxymethyl)-, (4S,5aS,6S,8R,9S,10S,11S,11aR,12R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 35523-89-8 HCAPLUS
CN 1H,10H-Pyrrolo[1,2-c]purine-10,10-diol, 2,6-diamino-4-[[(aminocarbonyl)oxy]methyl]-3a,4,8,9-tetrahydro-, (3aS,4R,10aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L59 ANSWER 3 OF 8 HCAPLUS COPYRIGHT 2003 ACS
AN 2002:408544 HCAPLUS
DN 136:406875

TI Pharmaceutical injections containing **sodium channel blocking** compounds
IN Kang, Yuhong; **Shum, Frank Haykong**
PA Nanning Maple Leaf Pharmaceutical Co., Ltd., Peop. Rep. China
SO PCT Int. Appl., 60 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM A61K045-00
ICS A61K031-4995; A61K031-519
CC 63-6 (Pharmaceuticals)
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2002041915	A1	20020530	WO 2001-CN1566	20011119
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	CN 1353990	A	20020619	CN 2000-132672	20001122
	US 2002119987	A1	20020829	US 2001-819796	20010329
	AU 2002021491	A5	20020603	AU 2002-21491	20011119
PRAI	CN 2000-132672	A	20001122		
	WO 2001-CN1566	W	20011119		

AB The compn. of the present invention comprises a **sodium channel blocking** compd. which is capable of specifically binding to a site, either on an SS1 region or an SS2 region, on an extracellular region of a **sodium channel** alpha subunit, and a pharmaceutically acceptable carrier. An injection contained **tetrodotoxin** 1.5, 0.5% acetic acid 0.1, propylene glycol 80, and water for injection 100 mL. Stability of **tetrodotoxin** against light, heat, and storage time was studied.

ST pharmaceutical injection **sodium channel blocker; tetrodotoxin** acetic acid propylene glycol pharmaceutical injection

IT Quaternary ammonium compounds, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(alkylbenzyldimethyl, chlorides; pharmaceutical injections contg. **sodium channel blocking** compds.)

IT Drug delivery systems
(injections; pharmaceutical injections contg. **sodium channel blocking** compds.)

IT Anti-inflammatory agents
(nonsteroidal; pharmaceutical injections contg. **sodium channel blocking** compds.)

IT Acids, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(org.; pharmaceutical injections contg. **sodium channel blocking** compds.)

IT Antibiotics
Buffers
Permeation enhancers
Vasoconstrictors
(pharmaceutical injections contg. **sodium channel blocking** compds.)

IT Amines, biological studies
Steroids, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(pharmaceutical injections contg. **sodium channel blocking** compds.)

IT **Ion channel blockers**
(**sodium**; pharmaceutical injections contg. **sodium channel blocking** compds.)

IT **4368-28-9, Tetrodotoxin**
RL: PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pharmaceutical injections contg. **sodium channel blocking** compds.)

IT 55-68-5, Phenylmercuric nitrate 56-81-5, Glycerine, biological studies 57-15-8, Chlorobutanol 57-55-6, Propylene glycol, biological studies 62-38-4, Phenylmercuric acetate 64-19-7, Acetic acid, biological studies 69-65-8, Mannitol 77-92-9, Citric acid, biological studies 107-21-1, 1,2-Ethanediol, biological studies 112-80-1, Oleic acid, biological studies 126-44-3, Citrate, biological studies **3270-35-7, Tetrodonic acid** 7647-01-0, Hydrochloric acid, biological studies 7647-14-5, **Sodium** chloride, biological studies **7724-38-1, Tetrodaminotoxin 7724-39-2, Methoxytetrodotoxin 7724-40-5, Ethoxytetrodotoxin 7724-41-6, Deoxytetrodotoxin 13072-89-4, Anhydrotetrodotoxin** 14213-97-9, Borate 14265-44-2, Phosphate, biological studies **35523-89-8, Saxitoxin**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pharmaceutical injections contg. **sodium channel blocking** compds.)

RE.CNT 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD

RE

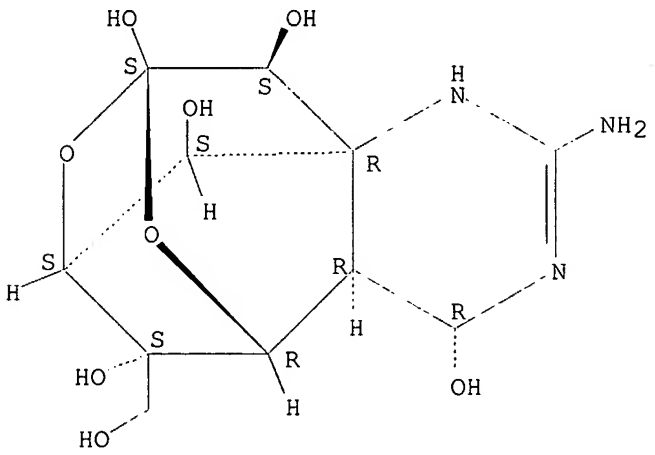
(1) Anon; US 3898339 A 1975 HCAPLUS
(2) Anon; WO 9524903 A 1995 HCAPLUS
(3) Anon; CN 1192903 A 1998 HCAPLUS
(4) Anon; US 6030974 A 2000 HCAPLUS

IT **4368-28-9, Tetrodotoxin**
RL: PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pharmaceutical injections contg. **sodium channel blocking** compds.)

RN 4368-28-9 HCAPLUS

CN 5,9:7,10a-Dimethano-10aH-[1,3]dioxocino[6,5-d]pyrimidine-4,7,10,11,12-pentol, octahydro-12-(hydroxymethyl)-2-imino-, (4R,4aR,5R,7S,9S,10S,10aR,11S,12S)- (9CI) (CA INDEX NAME)

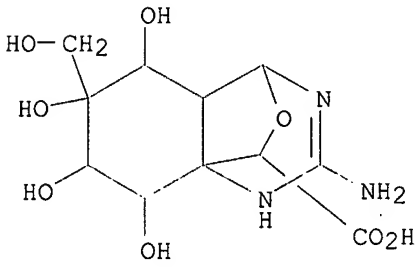
Absolute stereochemistry.



IT **3270-35-7, Tetrodonic acid 7724-38-1**
, Tetrodaminotoxin 7724-39-2,
Methoxytetrodotoxin 7724-40-5,
Ethoxytetrodotoxin 7724-41-6, Deoxytetrodotoxin
13072-89-4, Anhydrotetrodotoxin 35523-89-8,
Saxitoxin
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pharmaceutical injections contg. **sodium channel**
blocking compds.)

RN 3270-35-7 HCAPLUS

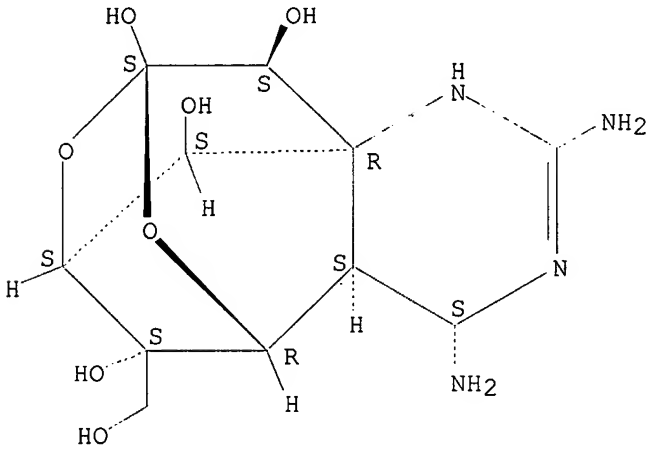
CN 1H-4,8a-(Epoxymethano)quinazoline-9-carboxylic acid, 2-amino-4,4a,5,6,7,8-hexahydro-5,6,7,8-tetrahydroxy-6-(hydroxymethyl)-, (4S,4aR,5R,6S,7R,8R,8aR,9R)- (9CI) (CA INDEX NAME)



RN 7724-38-1 HCAPLUS

CN 5,9:7,10a-Dimethano-10aH-[1,3]dioxocino[6,5-d]pyrimidine-7,10,11,12-tetrol, 4-aminooctahydro-12-(hydroxymethyl)-2-imino-, (4R,4aR,5R,7S,9S,10S,10aR,11S,12S)- (9CI) (CA INDEX NAME)

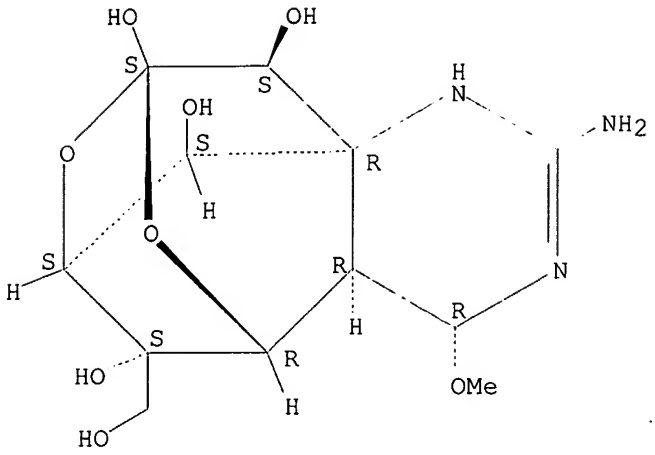
Absolute stereochemistry.



RN 7724-39-2 HCAPLUS

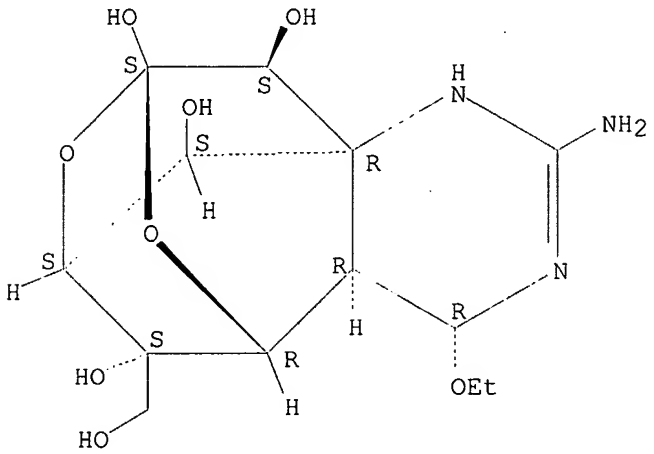
CN 5,9:7,10a-Dimethano-10aH-[1,3]dioxocino[6,5-d]pyrimidine-7,10,11,12-tetrol, octahydro-12-(hydroxymethyl)-2-imino-4-methoxy-, (4R,4aR,5R,7S,9S,10S,10aR,11S,12S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



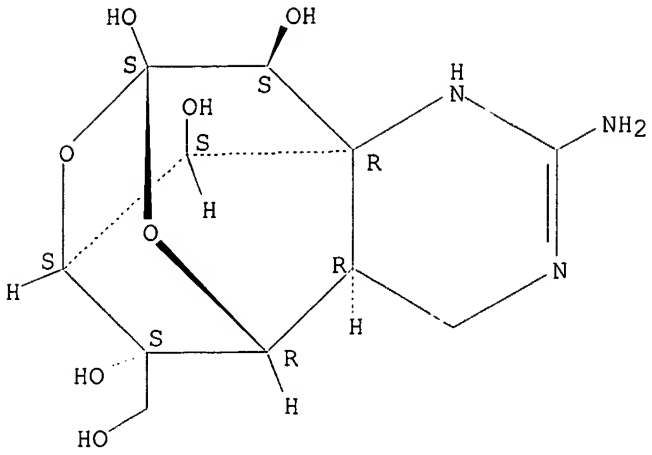
RN 7724-40-5 HCAPLUS
CN 5,9:7,10a-Dimethano-10aH-[1,3]dioxocino[6,5-d]pyrimidine-7,10,11,12-tetrol, 4-ethoxyoctahydro-12-(hydroxymethyl)-2-imino-, (4R,4aR,5R,7S,9S,10S,10aR,11S,12S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



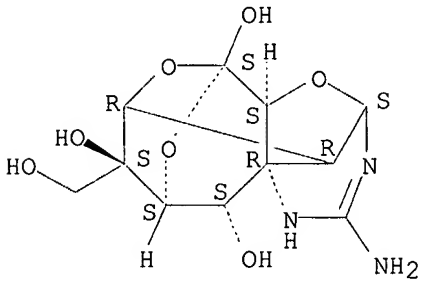
RN 7724-41-6 HCAPLUS
CN 5,9:7,10a-Dimethano-10aH-[1,3]dioxocino[6,5-d]pyrimidine-7,10,11,12-tetrol, 2-amino-1,4,4a,5,9,10-hexahydro-12-(hydroxymethyl)-, (4aR,5R,7S,9S,10S,10aR,11S,12S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



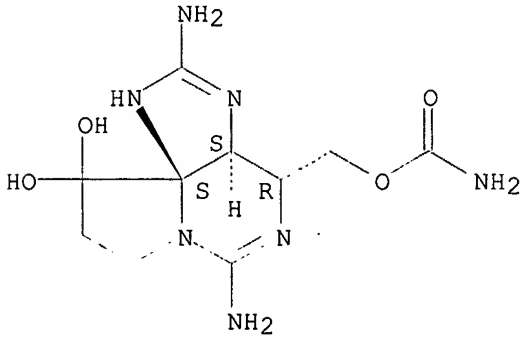
RN 13072-89-4 HCAPLUS
CN 6,10-Epoxy-4,8,11a-metheno-11aH-oxocino[4,3-f][1,3,5]oxadiazepine-6,9,11-triol, 2-amino-1,4,5a,6,8,9,10,11-octahydro-9-(hydroxymethyl)-, (4S,5aS,6S,8R,9S,10S,11S,11aR,12R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 35523-89-8 HCAPLUS
CN 1H,10H-Pyrrolo[1,2-c]purine-10,10-diol, 2,6-diamino-4-[[(aminocarbonyl)oxy]methyl]-3a,4,8,9-tetrahydro-, (3aS,4R,10aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L59 ANSWER 4 OF 8 HCAPLUS COPYRIGHT 2003 ACS
AN 2002:220374 HCAPLUS
DN 136:241691

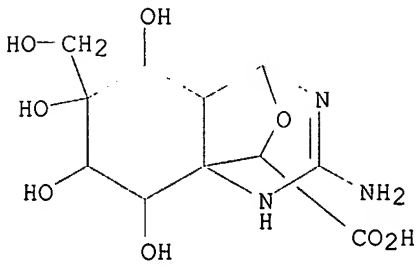
TI A method of analgesia using **sodium channel blockers**
IN Dong, Qingbin; **Shum, Frank Haykong**
PA WEX Medical Instrumentation Co., Peop. Rep. China
SO PCT Int. Appl., 60 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM A61K031-517
ICS A61P023-02; A61P025-04
CC 1-11 (Pharmacology)
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2002022129	A1	20020321	WO 2001-CN1391	20010911
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	CN 1356104	A	20020703	CN 2000-124517	20000918
	US 6407088	B1	20020618	US 2000-695053	20001025
	AU 2002013785	A5	20020326	AU 2002-13785	20010911
PRAI	CN 2000-124517	A	20000918		
	WO 2001-CN1391	W	20010911		

AB This invention relates to a method of producing analgesia in a mammal experiencing pain by systemically administering an effective amt. of a compn. comprising essentially of a **sodium channel blocking** compd., in a suitable pharmaceutical vehicle, to alleviate the pain.

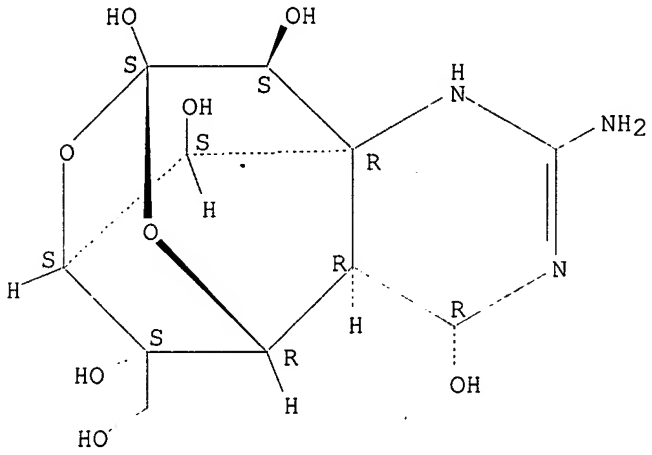
ST pain neuropathic cancer analgesia **sodium channel blocker**
IT Drug delivery systems
(aerosols; analgesia using **sodium channel blockers** for neuropathic and cancer pain)
IT Analgesics
Behavior
Drug withdrawal
Human
(analgesia using **sodium channel blockers** for neuropathic and cancer pain)
IT Drug delivery systems
(implants, osmotic pump; analgesia using **sodium channel blockers** for neuropathic and cancer pain)
IT Collagens, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(implants; analgesia using **sodium channel blockers** for neuropathic and cancer pain)
IT Drug delivery systems
(injections, i.m.; analgesia using **sodium channel blockers** for neuropathic and cancer pain)
IT Drug delivery systems
(injections, i.v.; analgesia using **sodium channel blockers** for neuropathic and cancer pain)
IT Drug delivery systems
(injections, s.c.; analgesia using **sodium channel blockers** for neuropathic and cancer pain)
IT Nerve, disease
(neuralgia; analgesia using **sodium channel**

blockers for neuropathic and cancer pain)
IT Drug delivery systems
(oral; analgesia using **sodium channel blockers** for neuropathic and cancer pain)
IT Drug delivery systems
(osmotic pumps, implants; analgesia using **sodium channel blockers** for neuropathic and cancer pain)
IT Neoplasm
(pain; analgesia using **sodium channel blockers** for neuropathic and cancer pain)
IT **Ion channel blockers**
(**sodium**; analgesia using **sodium channel blockers** for neuropathic and cancer pain)
IT Drug delivery systems
(sublingual; analgesia using **sodium channel blockers** for neuropathic and cancer pain)
IT Drug delivery systems
(suppositories; analgesia using **sodium channel blockers** for neuropathic and cancer pain)
IT Drug delivery systems
(tapes; analgesia using **sodium channel blockers** for neuropathic and cancer pain)
IT **3270-35-7, Tetrodonic acid 4368-28-9, Tetrodotoxin 7724-38-1, Tetrodaminotoxin 7724-39-2, Methoxytetrodotoxin 7724-40-5, Ethoxytetrodotoxin 7724-41-6, Deoxytetrodotoxin 13072-89-4, Anhydrotetrodotoxin 35523-89-8D, Saxitoxin**, hydroxy derivs. 64296-20-4, Neosaxitoxin
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(analgesia using **sodium channel blockers** for neuropathic and cancer pain)
RE.CNT 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE
(1) Anon; US 4022899 1977 HCAPLUS
(2) Anon; CN 1145225 A 1997 HCAPLUS
IT **3270-35-7, Tetrodonic acid 4368-28-9, Tetrodotoxin 7724-38-1, Tetrodaminotoxin 7724-39-2, Methoxytetrodotoxin 7724-40-5, Ethoxytetrodotoxin 7724-41-6, Deoxytetrodotoxin 13072-89-4, Anhydrotetrodotoxin 35523-89-8D, Saxitoxin**, hydroxy derivs.
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(analgesia using **sodium channel blockers** for neuropathic and cancer pain)
RN 3270-35-7 HCAPLUS
CN 1H-4,8a-(Epoxymethano)quinazoline-9-carboxylic acid, 2-amino-4,4a,5,6,7,8-hexahydro-5,6,7,8-tetrahydroxy-6-(hydroxymethyl)-, (4S,4aR,5R,6S,7R,8R,8aR,9R)- (9CI) (CA INDEX NAME)



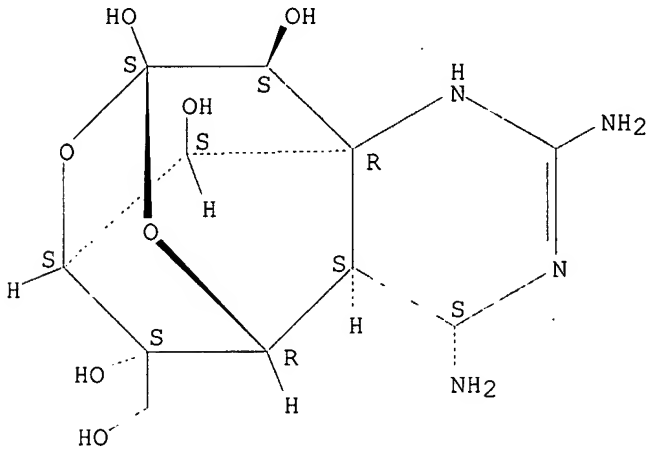
RN 4368-28-9 HCAPLUS
CN 5,9:7,10a-Dimethano-10aH-[1,3]dioxocino[6,5-d]pyrimidine-4,7,10,11,12-pentol, octahydro-12-(hydroxymethyl)-2-imino-, (4R,4aR,5R,7S,9S,10S,10aR,11S,12S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



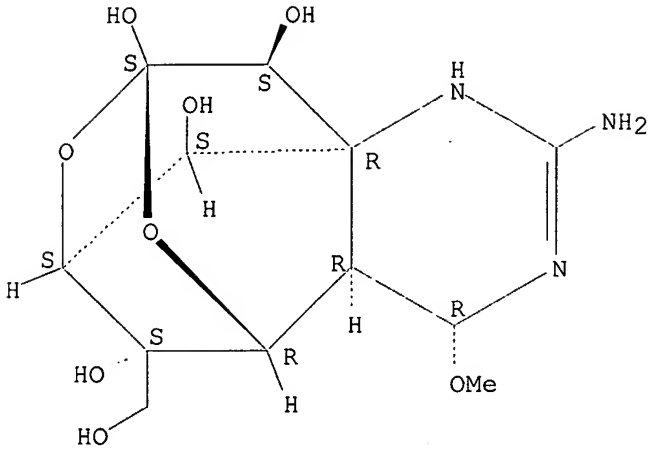
RN 7724-38-1 HCAPLUS
CN 5,9:7,10a-Dimethano-10aH-[1,3]dioxocino[6,5-d]pyrimidine-7,10,11,12-tetrol, 4-aminooctahydro-12-(hydroxymethyl)-2-imino-, (4R,4aR,5R,7S,9S,10S,10aR,11S,12S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



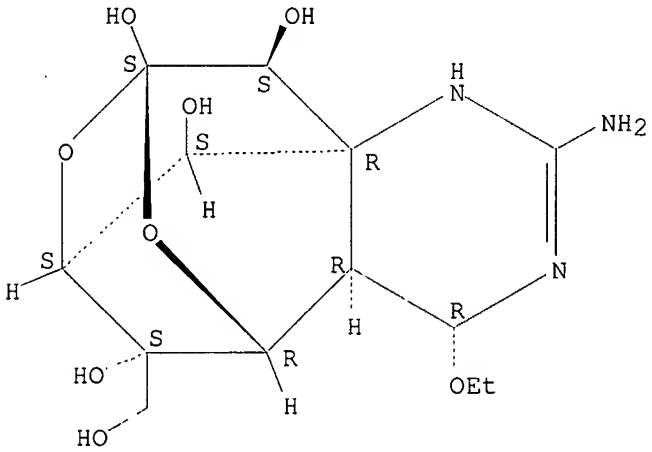
RN 7724-39-2 HCAPLUS
CN 5,9:7,10a-Dimethano-10aH-[1,3]dioxocino[6,5-d]pyrimidine-7,10,11,12-tetrol, octahydro-12-(hydroxymethyl)-2-imino-4-methoxy-, (4R,4aR,5R,7S,9S,10S,10aR,11S,12S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



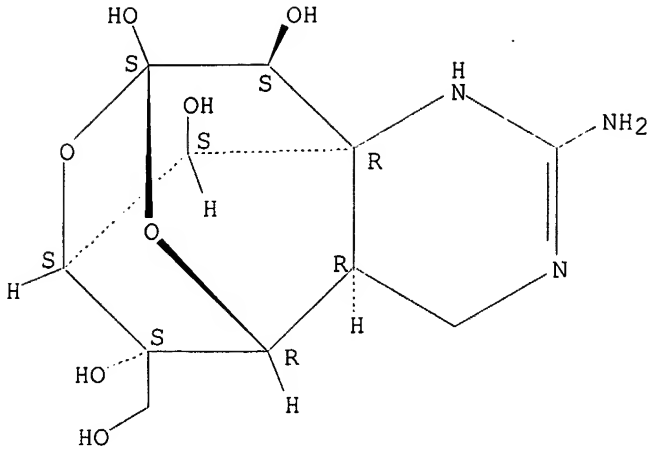
RN 7724-40-5 HCAPLUS
CN 5,9:7,10a-Dimethano-10aH-[1,3]dioxocino[6,5-d]pyrimidine-7,10,11,12-tetrol, 4-ethoxyoctahydro-12-(hydroxymethyl)-2-imino-, (4R,4aR,5R,7S,9S,10S,10aR,11S,12S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



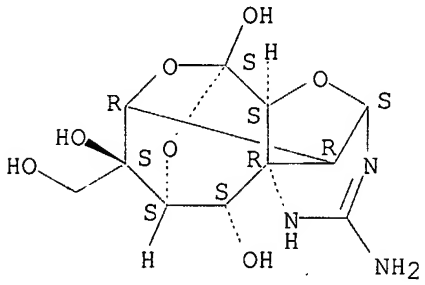
RN 7724-41-6 HCAPLUS
CN 5,9:7,10a-Dimethano-10aH-[1,3]dioxocino[6,5-d]pyrimidine-7,10,11,12-tetrol, 2-amino-1,4,4a,5,9,10-hexahydro-12-(hydroxymethyl)-, (4aR,5R,7S,9S,10S,10aR,11S,12S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



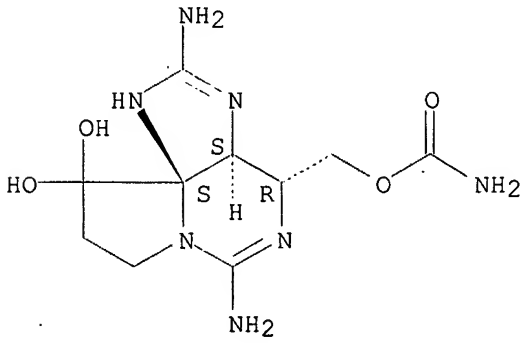
RN 13072-89-4 HCAPLUS
CN 6,10-Epoxy-4,8,11a-metheno-11aH-oxocino[4,3-f][1,3,5]oxadiazepine-6,9,11-triol, 2-amino-1,4,5a,6,8,9,10,11-octahydro-9-(hydroxymethyl)-, (4S,5aS,6S,8R,9S,10S,11S,11aR,12R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 35523-89-8 HCAPLUS
CN 1H,10H-Pyrrolo[1,2-c]purine-10,10-diol, 2,6-diamino-4-[[(aminocarbonyl)oxy]methyl]-3a,4,8,9-tetrahydro-, (3aS,4R,10aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L59 ANSWER 5 OF 8 HCAPLUS COPYRIGHT 2003 ACS
AN 2002:220373 HCAPLUS
DN 136:226808

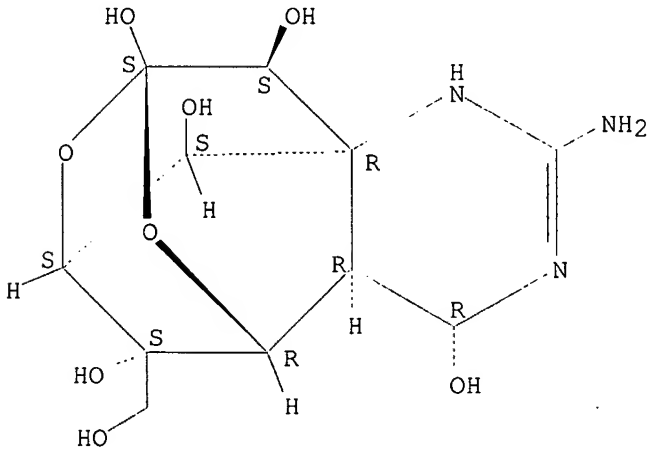
TI A method of local anesthesia and analgesia using **sodium channel blockers** and local anesthetics
IN **Ku, Baoshan**; Qi, Shiquan
PA WEX Medical Instrumentation Co., Ltd., Peop. Rep. China
SO PCT Int. Appl., 25 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM A61K031-517
ICS A61P023-02; A61P029-00
CC 1-11 (Pharmacology)
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2002022128	A1	20020321	WO 2001-CN1390	20010911
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	CN 1343491	A	20020410	CN 2000-124518	20000918
	AU 2002013784	A5	20020326	AU 2002-13784	20010911
PRAI	CN 2000-124518	A	20000918		
	WO 2001-CN1390	W	20010911		

AB The present invention provides a method of producing local analgesia and anesthesia in a mammal experiencing pain in a nerve tissue region. The method includes topically administering to the region, in a suitable pharmaceutical vehicle, an ED of a **sodium channel blocking** compd. in a pharmaceutically suitable vehicle.
ST neuropathic pain local anesthesia analgesia **sodium channel blocker**
IT Analgesics
Human
(local anesthesia and analgesia using **sodium channel blockers** and local anesthetics for neuropathic pain)
IT Anesthetics
(local; local anesthesia and analgesia using **sodium channel blockers** and local anesthetics for neuropathic pain)
IT Nerve, disease
(neuralgia; local anesthesia and analgesia using **sodium channel blockers** and local anesthetics for neuropathic pain)
IT Tooth
(pulp; local anesthesia and analgesia using **sodium channel blockers** and local anesthetics for neuropathic pain)
IT Nerve
(sciatic; local anesthesia and analgesia using **sodium channel blockers** and local anesthetics for neuropathic pain)
IT **Ion channel blockers**
(**sodium**; local anesthesia and analgesia using **sodium channel blockers** and local anesthetics for neuropathic pain)
IT Drug interactions
(synergistic; local anesthesia and analgesia using **sodium channel blockers** and local anesthetics for neuropathic pain)

IT Drug delivery systems
(topical; local anesthesia and analgesia using **sodium channel blockers** and local anesthetics for neuropathic pain)
IT Nerve
(trigeminal; local anesthesia and analgesia using **sodium channel blockers** and local anesthetics for neuropathic pain)
IT **4368-28-9, Tetrodotoxin**
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(local anesthesia and analgesia using **sodium channel blockers** and local anesthetics for neuropathic pain)
IT 59-46-1, Procaine 94-24-6, Tetracaine 137-58-6, Lidocaine **3270-35-7, Tetrodonic acid 7724-38-1, Tetrodaminotoxin 7724-39-2, Methoxytetrodotoxin 7724-40-5, Ethoxytetrodotoxin 7724-41-6, Deoxytetrodotoxin 13072-89-4, Anhydrotetrodotoxin**
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(local anesthesia and analgesia using **sodium channel blockers** and local anesthetics for neuropathic pain)
RE.CNT 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE
(1) Anon; CN 1145225 A 1977 HCAPLUS
(2) Anon; US 4022899 1997 HCAPLUS
IT **4368-28-9, Tetrodotoxin**
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(local anesthesia and analgesia using **sodium channel blockers** and local anesthetics for neuropathic pain)
RN 4368-28-9 HCAPLUS
CN 5,9:7,10a-Dimethano-10aH-[1,3]dioxocino[6,5-d]pyrimidine-4,7,10,11,12-pentol, octahydro-12-(hydroxymethyl)-2-imino-, (4R,4aR,5R,7S,9S,10S,10aR,11S,12S)- (9CI) (CA INDEX NAME)

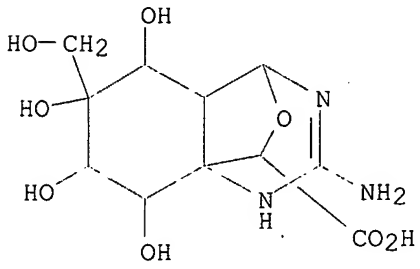
Absolute stereochemistry.



IT **3270-35-7, Tetrodonic acid 7724-38-1, Tetrodaminotoxin 7724-39-2, Methoxytetrodotoxin 7724-40-5, Ethoxytetrodotoxin 7724-41-6, Deoxytetrodotoxin 13072-89-4, Anhydrotetrodotoxin**
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL

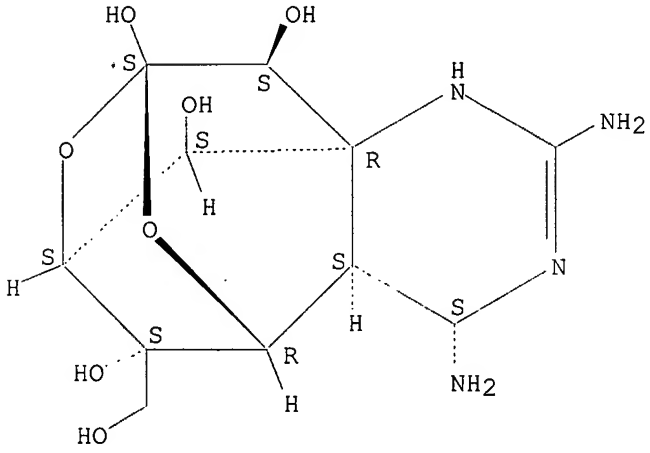
(Biological study); USES (Uses)
(local anesthesia and analgesia using **sodium channel blockers** and local anesthetics for neuropathic pain)

RN 3270-35-7 HCAPLUS
CN 1H-4,8a-(Epoxymethano)quinazoline-9-carboxylic acid, 2-amino-4,4a,5,6,7,8-hexahydro-5,6,7,8-tetrahydroxy-6-(hydroxymethyl)-, (4S,4aR,5R,6S,7R,8R,8aR,9R)- (9CI) (CA INDEX NAME)



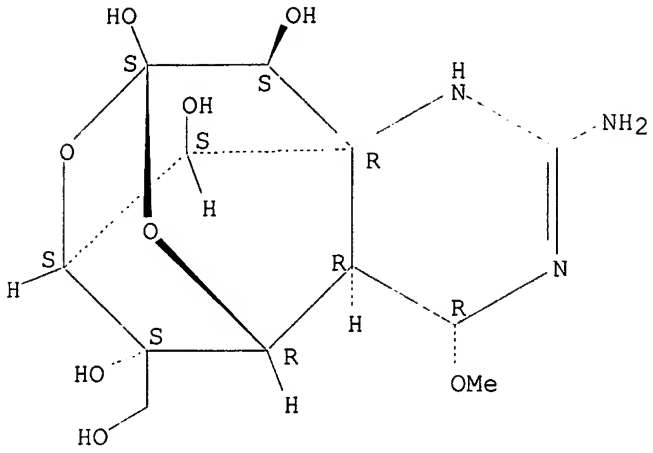
RN 7724-38-1 HCAPLUS
CN 5,9:7,10a-Dimethano-10aH-[1,3]dioxocino[6,5-d]pyrimidine-7,10,11,12-tetrol, 4-aminooctahydro-12-(hydroxymethyl)-2-imino-, (4R,4aR,5R,7S,9S,10S,10aR,11S,12S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



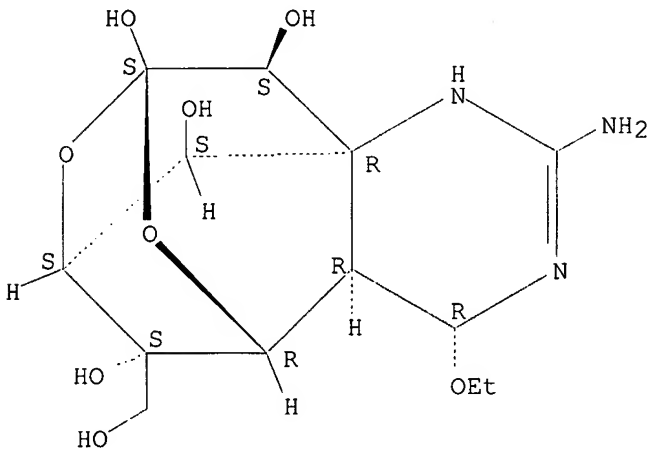
RN 7724-39-2 HCAPLUS
CN 5,9:7,10a-Dimethano-10aH-[1,3]dioxocino[6,5-d]pyrimidine-7,10,11,12-tetrol, octahydro-12-(hydroxymethyl)-2-imino-4-methoxy-, (4R,4aR,5R,7S,9S,10S,10aR,11S,12S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



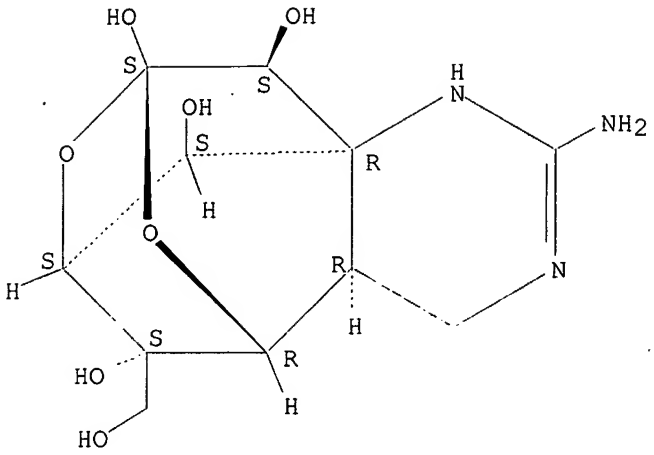
RN 7724-40-5 HCAPLUS
CN 5,9:7,10a-Dimethano-10aH-[1,3]dioxocino[6,5-d]pyrimidine-7,10,11,12-tetrol, 4-ethoxyoctahydro-12-(hydroxymethyl)-2-imino-, (4R,4aR,5R,7S,9S,10S,10aR,11S,12S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



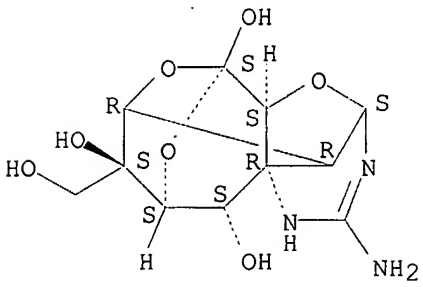
RN 7724-41-6 HCAPLUS
CN 5,9:7,10a-Dimethano-10aH-[1,3]dioxocino[6,5-d]pyrimidine-7,10,11,12-tetrol, 2-amino-1,4,4a,5,9,10-hexahydro-12-(hydroxymethyl)-, (4aR,5R,7S,9S,10S,10aR,11S,12S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 13072-89-4 HCAPLUS
CN 6,10-Epoxy-4,8,11a-metheno-11aH-oxocino[4,3-f][1,3,5]oxadiazepine-6,9,11-triol, 2-amino-1,4,5a,6,8,9,10,11-octahydro-9-(hydroxymethyl)-, (4S,5aS,6S,8R,9S,10S,11S,11aR,12R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L59 ANSWER 6 OF 8 HCAPLUS COPYRIGHT 2003 ACS
AN 2001:552385 HCAPLUS
DN 135:316858
TI Nociception and allodynia/hyperalgesia induced by intrathecal administration of fenvalerate
AU Kamei, Junzo; Sasaki, Mitsumasa; Zushida, Ko; Morita, Kayo; Tanaka, Shun-Ichi
CS Department of Pathophysiology & Therapeutics, Faculty of Pharmaceutical Sciences, Hoshi University, Tokyo, 142-8501, Japan
SO Japanese Journal of Pharmacology (2001), 86(3), 336-341
CODEN: JJPAAZ; ISSN: 0021-5198
PB Japanese Pharmacological Society
DT Journal
LA English
CC 14-10 (Mammalian Pathological Biochemistry)
cross-reference(s): 1
athecal injection of fenvalerate, a **Na channel**
r, at doses of 0.01 to 3 .mu.g, dose-dependently induced the
of a characteristic behavioral syndrome mainly consisting of
al hind limb scratching directed towards caudal parts of the body
ng or licking of the hind legs in mice. Fenvalerate-induced
was inhibited by **morphine** (1 - 10 mg/kg, i.p.). The
istic behavior was also inhibited by mexiletine, a **Na**
locker; MK-801, a N-methyl-D-aspartate ion-

channel blocker; and GR82334, a neurokinin-1-receptor antagonist. Calphostin C (3 pmol, i.t.), a protein kinase C inhibitor, inhibited fenvalerate-induced behavior. On the other hand, phorbol-12, 13-dibutyrate (50 pmol, i.t.), a protein kinase C activator, markedly **enhanced** the fenvalerate-induced behavior. The present results also showed that fenvalerate produced thermal allodynia and hyperalgesia in the tail-flick test. Furthermore, fenvalerate-induced thermal allodynia and hyperalgesia were inhibited by the pretreatment with calphostin C. These results suggest that the intrathecal administration of fenvalerate induces a marked nociceptive response and thermal allodynia/hyperalgesia, and they suggest that **tetrodotoxin** -resistant **Na channels** may play an important role in this effect.

ST fenvalerate nociception **tetrodotoxin** resistant **sodium channel**

IT Tachykinin receptors
(NK1 antagonists; fenvalerate induces nociception and allodynia/hyperalgesia in mice)

IT Glutamate antagonists
(NMDA antagonists; fenvalerate induces nociception and allodynia/hyperalgesia in mice)

IT Pain
Skin, disease
(allodynia; fenvalerate induces nociception and allodynia/hyperalgesia in mice)

IT Pain
(fenvalerate induces nociception and allodynia/hyperalgesia in mice)

IT Pain
(hyperalgesia; fenvalerate induces nociception and allodynia/hyperalgesia in mice)

IT **Ion channel blockers**
(**sodium**; fenvalerate induces nociception and allodynia/hyperalgesia in mice)

IT **Sodium channel**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(**tetrodotoxin**-resistant; fenvalerate induces nociception and allodynia/hyperalgesia in mice)

IT 121263-19-2, Calphostin C
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(effect of pretreatment with, on fenvalerate-induced nociception in mice)

IT **57-27-2, Morphine**, biological studies 31828-71-4, Mexiletine 77086-22-7, MK-801 129623-01-4, GR82334
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(effect of, on fenvalerate-induced nociception in mice)

IT 141436-78-4, Protein kinase C
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(effect of, on fenvalerate-induced nociception in mice)

IT 51630-58-1, Fenvalerate
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(fenvalerate induces nociception and allodynia/hyperalgesia in mice)

IT **4368-28-9, Tetrodotoxin**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(**tetrodotoxin-resistant Na channel**; fenvalerate induces nociception and allodynia/hyperalgesia in mice)

RE.CNT 41 THERE ARE 41 CITED REFERENCES AVAILABLE FOR THIS RECORD

RE

(1) Ahlgren, S; J Neurophysiol 1994, V72, P684 HCAPLUS
(2) Akopian, A; Nat Neurosci 1999, V2, P541 HCAPLUS
(3) Akopian, A; Nature 1996, V379, P257 HCAPLUS

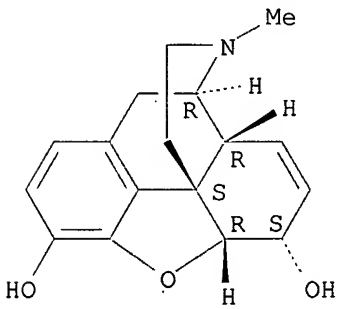
(4) Arbuckle, J; Neurosci Lett 1995, V185, P70 HCAPLUS
(5) Cardenas, C; J Neurosci 1997, V17, P7181 HCAPLUS
(6) Catterall, W; Annu Rev Pharmacol Toxicol 1980, V20, P15 HCAPLUS
(7) Cotton, J; J Biol Chem 1997, V272, P25617
(8) England, S; J Physiol 1996, V495, P429 HCAPLUS
(9) Gold, M; J Neurosci 1998, V18, P10345 HCAPLUS
(10) Gold, M; Proc Natl Acad Sci 1996, V93, P1108 HCAPLUS
(11) Gu, J; Nature 1997, V389, P749 HCAPLUS
(12) Hoehn, K; Neuron 1993, V10, P543 HCAPLUS
(13) Hylden, J; Brain Res 1981, V217, P212 HCAPLUS
(14) Hylden, J; Eur J Pharmacol 1980, V67, P313 HCAPLUS
(15) Jeftinija, S; Brain Res 1994, V639, P125 HCAPLUS
(16) Kamei, J; Jpn J Pharmacol 2000, V84, P89 HCAPLUS
(17) Kamei, J; Res Commun Chem Path Pharmacol 1992, V77, P245 HCAPLUS
(18) Kamei, J; Res Commun Chem Path Pharmacol 1993, V80, P153 HCAPLUS
(19) Khasar, S; Neuron 1990, V24, P253
(20) Khasar, S; Neurosci Lett 1998, V256, P17 HCAPLUS
(21) Kostyuk, P; Neuroscience 1981, V6, P2423 HCAPLUS
(22) Malmberg, A; Science 1997, V278, P279 HCAPLUS
(23) Mclean, M; Mol Cell Biochem 1988, V80, P95 HCAPLUS
(24) Narita, M; Neuroscience 1997, V76, P291 HCAPLUS
(25) Novakovic, S; J Neurosci 1998, V18, P2174 HCAPLUS
(26) Ogata, N; J Physiol 1993, V466, P9 HCAPLUS
(27) Ohsawa, M; Brain Res 1998, V803, P198 HCAPLUS
(28) Ohsawa, M; Eur J Pharmacol 1997, V339, P27 HCAPLUS
(29) Ohsawa, M; Eur J Pharmacol 1999, V372, P221 HCAPLUS
(30) Porecca, F; Proc Natl Acad Sci 1999, V96, P7640
(31) Portenoy, G; Pain 1990, V43, P273
(32) Rabert, D; Pain 1998, V78, P107 HCAPLUS
(33) Ritter, A; J Neurophysiol 1992, V68, P2033 HCAPLUS
(34) Sangameswaran, L; J Biol Chem 1996, V271, P5953 HCAPLUS
(35) Scholz, A; Pain 2000, V47, P47
(36) Song, J; Brain Res 1996, V708, P29 HCAPLUS
(37) Strassman, A; J Neurophysiol 1999, V81, P413 HCAPLUS
(38) Tasker, R; J Neurosurg 1992, V77, P373 MEDLINE
(39) Tate, S; Nat Neurosci 1998, V1, P653 HCAPLUS
(40) Thio, C; J Neurosci 1993, V13, P4889 HCAPLUS
(41) Yoshida, S; Cell Mol Neurobiol 1994, V14, P227 HCAPLUS

IT **57-27-2, Morphine**, biological studies
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(effect of, on fenvalerate-induced nociception in mice)

RN 57-27-2 HCAPLUS

CN Morphinan-3,6-diol, 7,8-didehydro-4,5-epoxy-17-methyl-, (5.alpha.,6.alpha.)- (9CI) (CA INDEX NAME)

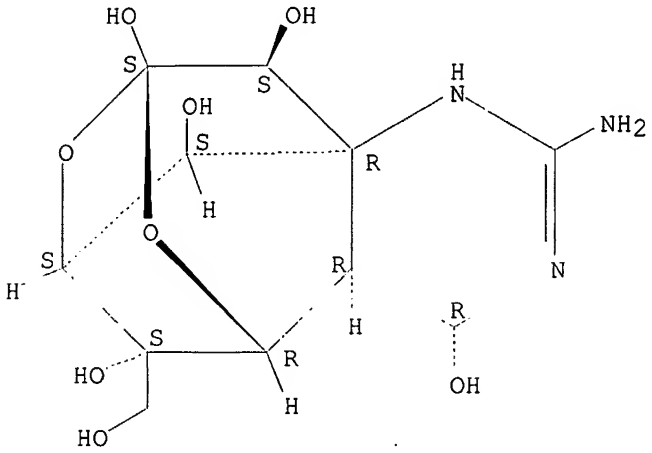
Absolute stereochemistry. Rotation (-).



IT **4368-28-9, Tetrodotoxin**
RL: BSU (Biological study, unclassified); BIOL (Biological study)

(**tetrodotoxin**-resistant **Na channel**;
fenvalerate induces nociception and allodynia/hyperalgesia in mice)
RN 4368-28-9 HCAPLUS
CN 5,9:7,10a-Dimethano-10aH-[1,3]dioxocino[6,5-d]pyrimidine-4,7,10,11,12-pentol, octahydro-12-(hydroxymethyl)-2-imino-, (4R,4aR,5R,7S,9S,10S,10aR,11S,12S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L59 ANSWER 7 OF 8 HCAPLUS COPYRIGHT 2003 ACS
AN **2001:489224** HCAPLUS
DN **135:97445**
TI Method for relieving pain associated with an internal disease site
IN Luiken, George A.
PA Fluoro Probe, Inc., USA
SO PCT Int. Appl., 31 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM A61K031-00
CC 63-6 (Pharmaceuticals)
Section cross-reference(s): 1
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2001047512	A2	20010705	WO 2000-US42661	20001206
WO 2001047512	A3	20020502		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRAI US 1999-457498 A1 19991208
AB Methods are provided for in vivo administration of a pain-relieving drug, such as a local anesthetic (e.g. lidocaine), to an interior disease site for pain relief at the interior disease site. In the invention pain treatment methods, a subject is administered a targeting construct comprising a biol. compatible pain-relieving agent and a tumor-avid ligand or monoclonal antibody that preponderantly binds to or is taken up by the tissue assocd. with an interior disease site. Administration is by a

method other than topical injection or application, such as parenteral injection. Because the pain-relieving agent is delivered by the ligand to the disease site, intractable pain situated in the interior of the body, such as is caused by various tumors, can be managed using a lower level of the pain-relieving agent then is required when the pain-relieving agent is injected in the free state.

ST tumor targeting pain relieving antibody conjugate

IT Chromogranins
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(A; pain-relieving agent-tumor avid ligand or antibody constructs for targeting internal disease site)

IT Antigens
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(CA 15-3, antibody to; pain-relieving agent-tumor avid ligand or antibody constructs for targeting internal disease site)

IT Immunoglobulin receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(IgE type II, antibody to; pain-relieving agent-tumor avid ligand or antibody constructs for targeting internal disease site)

IT Antigens
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(TAG-72 (tumor-assocd. glycoprotein 72), antibody to; pain-relieving agent-tumor avid ligand or antibody constructs for targeting internal disease site)

IT CA 125 (carbohydrate antigen)
CA19-9 antigen
CD19 (antigen)
CD20 (antigen)
CD22 (antigen)
CD45 (antigen)
CD5 (antigen)
Carcinoembryonic antigen
Epidermal growth factor receptors
Estrogen receptors
Mucins
Progesterone receptors
Prostate-specific antigen
.alpha.-Fetoproteins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(antibody to; pain-relieving agent-tumor avid ligand or antibody constructs for targeting internal disease site)

IT CD30 (antigen)
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(antibody to; pain-relieving agent-tumor avid ligand or antibody constructs for targeting internal disease site)

IT Peptides, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(binding hormone receptors, ligands; pain-relieving agent-tumor avid ligand or antibody constructs for targeting internal disease site)

IT Toxoids
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(botulin; pain-relieving agent-tumor avid ligand or antibody constructs for targeting internal disease site)

IT Gene, animal
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(c-erbB2, antibody to; pain-relieving agent-tumor avid ligand or antibody constructs for targeting internal disease site)

IT Antiarrhythmics
(class I; pain-relieving agent-tumor avid ligand or antibody constructs for targeting internal disease site)

IT Intestine, neoplasm
(colon; pain-relieving agent-tumor avid ligand or antibody constructs for targeting internal disease site)

IT Intestine, neoplasm
(colorectal; pain-relieving agent-tumor avid ligand or antibody constructs for targeting internal disease site)
IT Immunoglobulins
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(fragments; pain-relieving agent-tumor avid ligand or antibody constructs for targeting internal disease site)
IT Drug delivery systems
(injections, i.v.; pain-relieving agent-tumor avid ligand or antibody constructs for targeting internal disease site)
IT Anesthetics
(local; pain-relieving agent-tumor avid ligand or antibody constructs for targeting internal disease site)
IT Antibodies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(monoclonal; pain-relieving agent-tumor avid ligand or antibody constructs for targeting internal disease site)
IT Bladder
Endocrine system
Head
Mammary gland
Neck, anatomical
Pituitary gland
Prostate gland
(neoplasm; pain-relieving agent-tumor avid ligand or antibody constructs for targeting internal disease site)
IT Nerve, neoplasm
(neuroblastoma; pain-relieving agent-tumor avid ligand or antibody constructs for targeting internal disease site)
IT Endocrine system
(neuroendocrine system, neoplasm; pain-relieving agent-tumor avid ligand or antibody constructs for targeting internal disease site)
IT Lymphoma
(non-Hodgkin's; pain-relieving agent-tumor avid ligand or antibody constructs for targeting internal disease site)
IT Lung, neoplasm
(non-small-cell carcinoma; pain-relieving agent-tumor avid ligand or antibody constructs for targeting internal disease site)
IT Analgesia
Anticonvulsants
Brain, neoplasm
Carcinoid
Drug targeting
Hodgkin's disease
Liver, neoplasm
Melanoma
Multiple myeloma
Nicotinic agonists
Ovary, neoplasm
Pancreas, neoplasm
Sarcoma
Testis, neoplasm
Thyroid gland, neoplasm
Uterus, neoplasm
(pain-relieving agent-tumor avid ligand or antibody constructs for targeting internal disease site)
IT Hormones, animal, biological studies
Opioids
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pain-relieving agent-tumor avid ligand or antibody constructs for targeting internal disease site)
IT Growth hormone receptors
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(peptides binding to, ligands; pain-relieving agent-tumor avid ligand or antibody constructs for targeting internal disease site)

IT Lung, neoplasm
(small-cell carcinoma; pain-relieving agent-tumor avid ligand or antibody constructs for targeting internal disease site)

IT **Ion channel blockers**
(**sodium**; pain-relieving agent-tumor avid ligand or antibody constructs for targeting internal disease site)

IT Antigens
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(tumor-assocd., antibody to; pain-relieving agent-tumor avid ligand or antibody constructs for targeting internal disease site)

IT Proteins, specific or class
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(tumor-specific, antibody to; pain-relieving agent-tumor avid ligand or antibody constructs for targeting internal disease site)

IT 9002-61-3, Human chorionic gonadotropin
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(antibody to; pain-relieving agent-tumor avid ligand or antibody constructs for targeting internal disease site)

IT 69-78-3 2831-66-5 68181-17-9 72252-96-1 106145-13-5 115616-51-8 150244-18-1 158913-22-5 160854-54-6 204713-28-0
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(crosslinking agent; pain-relieving agent-tumor avid ligand or antibody constructs for targeting internal disease site)

IT 329900-75-6
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(inhibitors; pain-relieving agent-tumor avid ligand or antibody constructs for targeting internal disease site)

IT 7658-08-4 51110-01-1, Somatostatin
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(ligand; pain-relieving agent-tumor avid ligand or antibody constructs for targeting internal disease site)

IT 2543-43-3 130838-28-7 150243-58-6 150243-59-7 153177-60-7 256504-33-3 256504-34-4 256504-35-5 256504-36-6
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(linker moiety; pain-relieving agent-tumor avid ligand or antibody constructs for targeting internal disease site)

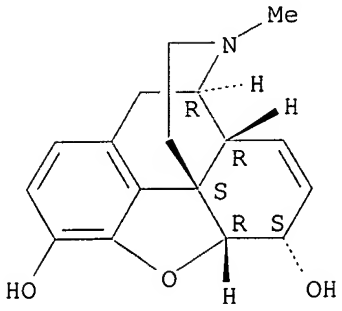
IT **57-27-2**, **Morphine**, biological studies 57-42-1, Meperidine 59-46-1, Procaine 63-68-3, Methionine, biological studies 76-42-6, Oxycodone **76-99-3**, **Methadone** 85-79-0, Dibucaine 94-24-6, Tetracaine 96-88-8, Mepivacaine 125-28-0, Dihydrocodeine 125-29-1, Hydrocodone 133-16-4, Chloroprocaine 136-47-0 137-58-6, Lidocaine 466-99-9, Hydromorphone 509-60-4, Dihydromorphine 561-27-3, Heroin 721-50-6, Prilocaine 22264-50-2, 1-aminocyclobutane-1-carboxylic acid 36637-18-0, Etidocaine 38396-39-3, Bupivacaine 52485-79-7, Buprenorphine 60142-96-3, Gabapentin 66532-85-2, Propacetamol 83150-76-9, Octreotide 84057-95-4, Ropivacaine 107452-89-1, Ziconotide 108736-35-2, Lanreotide 113775-47-6, Dexmedetomidine 161982-62-3, P829 264596-75-0, P587
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pain-relieving agent-tumor avid ligand or antibody constructs for targeting internal disease site)

IT **57-27-2**, **Morphine**, biological studies **76-99-3**, **Methadone**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pain-relieving agent-tumor avid ligand or antibody constructs for targeting internal disease site)

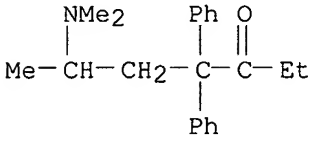
RN 57-27-2 HCAPLUS

CN Morphinan-3,6-diol, 7,8-didehydro-4,5-epoxy-17-methyl-, (5.alpha.,6.alpha.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



RN 76-99-3 HCAPLUS
CN 3-Heptanone, 6-(dimethylamino)-4,4-diphenyl- (7CI, 8CI, 9CI) (CA INDEX NAME)



L59 ANSWER 8 OF 8 HCAPLUS COPYRIGHT 2003 ACS
AN **1992:440075** HCAPLUS
DN **117:40075**
TI Cardiac instability amplified by use-dependent **sodium channel blockade**
AU Starmer, C. Frank; Lancaster, Alisa R.; Lastra, Anselmo A.; Grant, Augustus O.
CS Med. Cent., Duke Univ., Durham, NC, 27710, USA
SO American Journal of Physiology (1992), 262(4, Pt. 2), H1305-H1310
CODEN: AJPHAP; ISSN: 0002-9513
DT Journal
LA English
CC 1-8 (Pharmacology)
AB Drugs that exhibit use-dependent **Na channel blockade**, including antiarrhythmic agents, tricyclic antidepressants, **opiate**-like analgesics, and cocaine, are linked with an increased susceptibility to cardiac arrhythmias and sudden death. Computer simulations indicate that **Na channel blockade** retards recovery of excitability, thereby increasing the spatial dispersion of refractoriness, a precursor of many cardiac arrhythmias. In isolated rabbit left atria, stimuli timed to occur at increasing intervals following conditioning stimuli reveal an unstable interval (vulnerable period) during which single stimuli initiate trains of responses. The vulnerable period is extended by use-dependent **Na channel blockade** and provides a model for assaying proarrhythmic potential and probing cardiac instability.
ST heart arrhythmia **sodium channel blocker**
IT **Opioids**
RL: BIOL (Biological study)
(analgesics, heart arrhythmia induction by, mechanism of)
IT Antiarrhythmics
(heart arrhythmia from, evaluation of)
IT Toxicity
(of drugs, heart arrhythmia in, mechanism of)
IT Analgesics

(**opiates**, heart arrhythmia induction by, mechanism of)
IT Antidepressants
(tricyclic, heart arrhythmia induction by, mechanism of)
IT Heart, disease
(arrhythmia, from **sodium channel blockers**
, mechanism of)
IT **Ion channel blockers**
(**sodium**, heart arrhythmia from, mechanism of)
IT 50-36-2, Cocaine 137-58-6, Lidocaine
RL: BIOL (Biological study)
(heart arrhythmia from, evaluation of)

=> fil reg
FILE 'REGISTRY' ENTERED AT 09:54:14 ON 05 MAR 2003
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

Property values tagged with IC are from the ZIC/VINITI data file
provided by InfoChem.

STRUCTURE FILE UPDATES: 3 MAR 2003 HIGHEST RN 496834-05-0
DICTIONARY FILE UPDATES: 3 MAR 2003 HIGHEST RN 496834-05-0

TSCA INFORMATION NOW CURRENT THROUGH MAY 20, 2002

Please note that search-term pricing does apply when
conducting SmartSELECT searches.

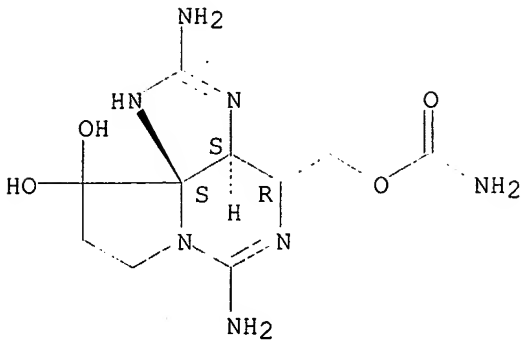
Crossover limits have been increased. See HELP CROSSOVER for details.

Experimental and calculated property data are now available. See HELP
PROPERTIES for more information. See STNote 27, Searching Properties
in the CAS Registry File, for complete details:
http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf

=> d ide can tot l60

L60 ANSWER 1 OF 13 REGISTRY COPYRIGHT 2003 ACS
RN **35523-89-8** REGISTRY
CN 1H,10H-Pyrrolo[1,2-c]purine-10,10-diol, 2,6-diamino-4-
[[(aminocarbonyl)oxy]methyl]-3a,4,8,9-tetrahydro-, (3aS,4R,10aS)- (9CI)
(CA INDEX NAME)
OTHER CA INDEX NAMES:
CN 1H,10H-Pyrrolo[1,2-c]purine-10,10-diol, 2,6-diamino-4-
[[(aminocarbonyl)oxy]methyl]-3a,4,8,9-tetrahydro-, [3aS-
(3a.alpha.,4.alpha.,10aR*)]-
CN Saxitoxin (7CI, 8CI)
OTHER NAMES:
CN (+)-Saxitoxin
CN Saxitoxin hydrate
CN STX
FS STEREOSEARCH
DR 11017-04-2, 55803-44-6, 51938-46-6
MF C10 H17 N7 O4
CI COM
LC STN Files: ADISNEWS, AGRICOLA, ANABSTR, BEILSTEIN*, BIOBUSINESS, BIOSIS,
BIOTECHNO, CA, CANCERLIT, CAOLD, CAPLUS, CEN, CSCHEM, DDFU, DRUGU,
EMBASE, IFICDB, IFIPAT, IFIUDB, MEDLINE, NAPRALERT, NIOSHTIC, PROMT,
RTECS*, TOXCENTER, ULIDAT, USPATFULL
(*File contains numerically searchable property data)

Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

798 REFERENCES IN FILE CA (1962 TO DATE)
38 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
799 REFERENCES IN FILE CAPLUS (1962 TO DATE)
4 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

REFERENCE 1: 138:132294

REFERENCE 2: 138:132287

REFERENCE 3: 138:118720

REFERENCE 4: 138:118718

REFERENCE 5: 138:102233

REFERENCE 6: 138:102105

REFERENCE 7: 138:88656

REFERENCE 8: 138:84812

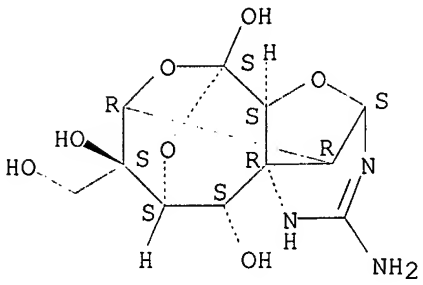
REFERENCE 9: 138:83128

REFERENCE 10: 138:34253

L60 ANSWER 2 OF 13 REGISTRY COPYRIGHT 2003 ACS
RN **13072-89-4** REGISTRY
CN 6,10-Epoxy-4,8,11a-metheno-11aH-oxocino[4,3-f][1,3,5]oxadiazepine-6,9,11-triol, 2-amino-1,4,5a,6,8,9,10,11-octahydro-9-(hydroxymethyl)-, (4S,5aS,6S,8R,9S,10S,11S,11aR,12R)- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Tetrodotoxin, 4,9-anhydro- (8CI)
CN Tetrodotoxin, 4,9-dideoxy-4,9-epoxy-, (4.beta.,9.beta.)-
CN Tetrodotoxin, anhydro- (7CI)
OTHER NAMES:
CN 4,9-Anhydrotetrodotoxin
CN Anhydroepitetrodotoxin
CN Anhydrotetrodotoxin
FS STEREOSEARCH
DR 7724-36-9, 16998-61-1, 17289-89-3, 2054-43-5
MF C11 H15 N3 O7
CI COM

LC STN Files: AGRICOLA, ANABSTR, BEILSTEIN*, BIOSIS, CA, CAOLD, CAPLUS, CASREACT, MEDLINE, NAPRALERT, RTECS*, TOXCENTER, USPATFULL
(*File contains numerically searchable property data)

Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

85 REFERENCES IN FILE CA (1962 TO DATE)
85 REFERENCES IN FILE CAPLUS (1962 TO DATE)
3 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

REFERENCE 1: 138:38538

REFERENCE 2: 137:363099

REFERENCE 3: 137:336926

REFERENCE 4: 137:304801

REFERENCE 5: 137:227949

REFERENCE 6: 137:180989

REFERENCE 7: 137:92915

REFERENCE 8: 137:63423

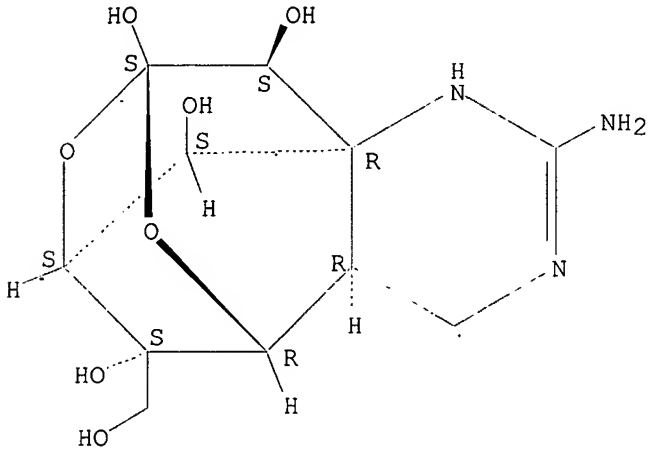
REFERENCE 9: 137:58860

REFERENCE 10: 137:1763

L60 ANSWER 3 OF 13 REGISTRY COPYRIGHT 2003 ACS
RN **7724-41-6** REGISTRY
CN 5,9:7,10a-Dimethano-10aH-[1,3]dioxocino[6,5-d]pyrimidine-7,10,11,12-tetrol, 2-amino-1,4,4a,5,9,10-hexahydro-12-(hydroxymethyl)-, (4aR,5R,7S,9S,10S,10aR,11S,12S)- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN 5,9:7,10a-Dimethano-10aH-[1,3]dioxocino[6,5-d]pyrimidine-7,10,11,12-tetrol, octahydro-12-(hydroxymethyl)-2-imino-, [4aR-(4a.alpha.,5.alpha.,7.alpha.,9.alpha.,10.alpha.,10a.beta.,11S*,12S*)]-
CN Tetrodotoxin, 4-deoxy- (8CI)
CN Tetrodotoxin, deoxy- (7CI)
OTHER NAMES:
CN Deoxytetrodotoxin
CN Desoxytetrodotoxin
FS STEREOSEARCH
DR 16813-05-1, 17289-92-8

MF C11 H17 N3 O7
LC STN Files: BEILSTEIN*, CA, CAOLD, CAPLUS, IFICDB, IFIPAT, IFIUDB, RTECS*, TOXCENTER, USPATFULL
(*File contains numerically searchable property data)

Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

21 REFERENCES IN FILE CA (1962 TO DATE)
21 REFERENCES IN FILE CAPLUS (1962 TO DATE)
3 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

REFERENCE 1: 138:38538

REFERENCE 2: 137:363099

REFERENCE 3: 137:304801

REFERENCE 4: 136:406875

REFERENCE 5: 136:241691

REFERENCE 6: 136:226808

REFERENCE 7: 135:56081

REFERENCE 8: 135:41024

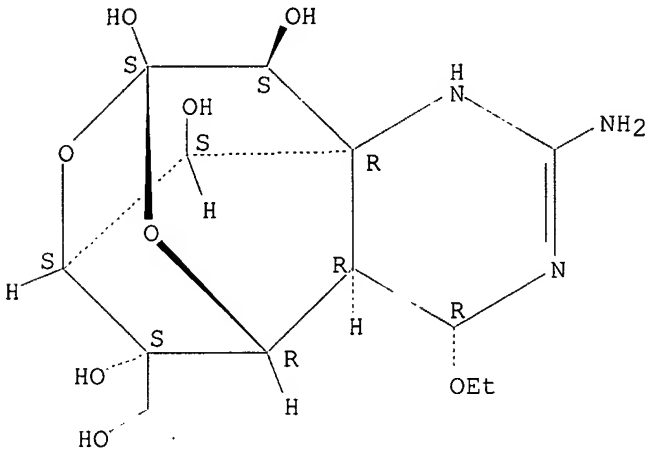
REFERENCE 9: 128:303619

REFERENCE 10: 128:252536

L60 ANSWER 4 OF 13 REGISTRY COPYRIGHT 2003 ACS
RN **7724-40-5** REGISTRY
CN 5,9:7,10a-Dimethano-10aH-[1,3]dioxocino[6,5-d]pyrimidine-7,10,11,12-tetrol, 4-ethoxyoctahydro-12-(hydroxymethyl)-2-imino-, (4R,4aR,5R,7S,9S,10S,10aR,11S,12S)- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Tetrodotoxin, O4-ethyl- (7CI, 8CI)
OTHER NAMES:
CN 4-Ethoxytetrodotoxin

CN Ethoxytetrodotoxin
FS STEREOSEARCH
DR 16846-39-2
MF C13 H21 N3 O8
LC STN Files: BEILSTEIN*, CA, CAOLD, CAPLUS, RTECS*, TOXCENTER, USPATFULL
(*File contains numerically searchable property data)

Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

7 REFERENCES IN FILE CA (1962 TO DATE)
7 REFERENCES IN FILE CAPLUS (1962 TO DATE)
3 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

REFERENCE 1: 137:363099

REFERENCE 2: 137:304801

REFERENCE 3: 136:406875

REFERENCE 4: 136:241691

REFERENCE 5: 136:226808

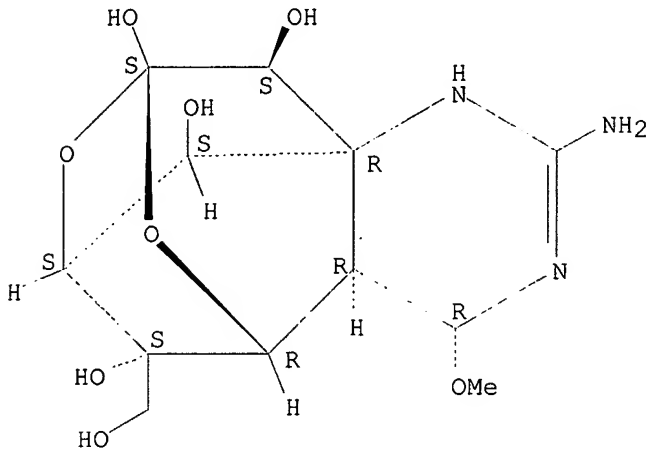
REFERENCE 6: 128:303619

REFERENCE 7: 128:252536

L60 ANSWER 5 OF 13 REGISTRY COPYRIGHT 2003 ACS
RN **7724-39-2** REGISTRY
CN 5,9:7,10a-Dimethano-10aH-[1,3]dioxocino[6,5-d]pyrimidine-7,10,11,12-tetrol, octahydro-12-(hydroxymethyl)-2-imino-4-methoxy-, (4R,4aR,5R,7S,9S,10S,10aR,11S,12S)- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Tetrodotoxin, O4-methyl-
OTHER NAMES:
CN 4-Methoxytetrodotoxin
CN 4-O-Methyltetrodotoxin
CN Methoxytetrodotoxin
FS STEREOSEARCH
DR 16846-38-1, 17289-93-9

MF C12 H19 N3 O8
LC STN Files: BEILSTEIN*, CA, CAOLD, CAPLUS, RTECS*, TOXCENTER, USPATFULL
(*File contains numerically searchable property data)

Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

7 REFERENCES IN FILE CA (1962 TO DATE)
7 REFERENCES IN FILE CAPLUS (1962 TO DATE)
1 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

REFERENCE 1: 137:363099

REFERENCE 2: 137:304801

REFERENCE 3: 136:406875

REFERENCE 4: 136:241691

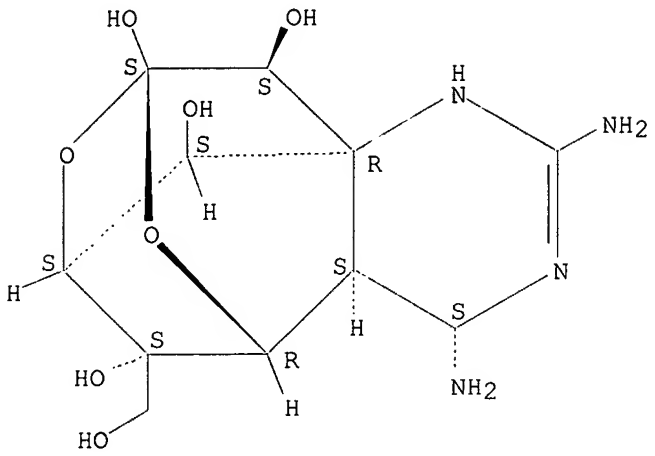
REFERENCE 5: 136:226808

REFERENCE 6: 128:303619

REFERENCE 7: 128:252536

L60 ANSWER 6 OF 13 REGISTRY COPYRIGHT 2003 ACS
RN **7724-38-1** REGISTRY
CN 5,9:7,10a-Dimethano-10aH-[1,3]dioxocino[6,5-d]pyrimidine-7,10,11,12-tetrol, 4-aminooctahydro-12-(hydroxymethyl)-2-imino-, (4R,4aR,5R,7S,9S,10S,10aR,11S,12S)- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Tetrodotoxin, 4-amino-4-deoxy-, (4.alpha.)- (8CI)
OTHER NAMES:
CN 4-Aminodeoxytetrodotoxin
CN Tetrodaminotoxin
FS STEREOSEARCH
DR 16998-62-2, 17289-94-0, 2054-84-4
MF C11 H18 N4 O7
LC STN Files: BEILSTEIN*, CA, CAOLD, CAPLUS, RTECS*, TOXCENTER, USPATFULL
(*File contains numerically searchable property data)

Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

14 REFERENCES IN FILE CA (1962 TO DATE)
14 REFERENCES IN FILE CAPLUS (1962 TO DATE)
1 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

REFERENCE 1: 137:363099

REFERENCE 2: 137:304801

REFERENCE 3: 136:406875

REFERENCE 4: 136:241691

REFERENCE 5: 136:226808

REFERENCE 6: 128:252536

REFERENCE 7: 121:99052

REFERENCE 8: 67:89145

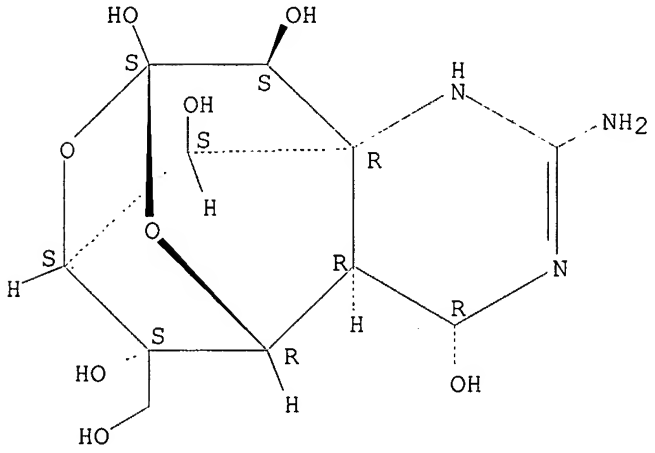
REFERENCE 9: 65:13482

REFERENCE 10: 65:13481

L60 ANSWER 7 OF 13 REGISTRY COPYRIGHT 2003 ACS
RN **4368-28-9** REGISTRY
CN 5,9:7,10a-Dimethano-10aH-[1,3]dioxocino[6,5-d]pyrimidine-4,7,10,11,12-pentol, octahydro-12-(hydroxymethyl)-2-imino-, (4R,4aR,5R,7S,9S,10S,10aR,11S,12S)- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN 8a(1H)-Quinazolineorthoglycolic acid, octahydro-4,5,6,7,8-pentahydroxy-6-(hydroxymethyl)-2-imino-, cyclic 8a,5:8a,7-ester (7CI)
CN Tetrodotoxin (8CI)
OTHER NAMES:
CN (-)-Tetrodotoxin
CN 5,9:7,10a-Dimethano-10aH-[1,3]dioxocino[6,5-d]pyrimidine-4,7,10,11,12-pentol, octahydro-12-(hydroxymethyl)-2-imino-, [4R-(4.alpha.,4a.alpha.,5.alpha.,7.alpha.,9.alpha.,10.alpha.,10a.beta.,11S*,12

S*)]-
CN Araregai toxin
CN Babylonia japonica toxin 1
CN BJT 1
CN Maculotoxin
CN Spheroidine
CN Tarichatoxin
CN Tetrodotoxine
CN TTX
CN [4R-(4.alpha.,4a.alpha.,5.alpha.,7.alpha.,9.alpha.,10.alpha.,10a.beta.,11S*,12S*)]-Octahydro-12-(hydroxymethyl)-2-imino-5,9:7,10a-dimethano-10aH-[1,3]dioxocino[6,5-d]pyrimidine-4,7,10,11,12-pentol
FS STEREOSEARCH
DR 12626-86-7, 9014-39-5, 11005-69-9, 11026-09-8, 17289-88-2, 2229-61-0
MF C11 H17 N3 O8
CI COM
LC STN Files: ADISNEWS, AGRICOLA, ANABSTR, BEILSTEIN*, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CABA, CANCERLIT, CAOLD, CAPLUS, CASREACT, CHEMCATS, CHEMLIST, CIN, CSCHEM, DDFU, DRUGU, EMBASE, HSDB*, IFICDB, IFIPAT, IFIUDB, IPA, MEDLINE, MRCK*, NAPRALERT, NIOSHTIC, PROMT, RTECS*, TOXCENTER, USPAT2, USPATFULL
(*File contains numerically searchable property data)
Other Sources: EINECS**
(**Enter CHEMLIST File for up-to-date regulatory information)

Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

2153 REFERENCES IN FILE CA (1962 TO DATE)
32 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
2153 REFERENCES IN FILE CAPLUS (1962 TO DATE)
9 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

REFERENCE 1: 138:119602

REFERENCE 2: 138:118729

REFERENCE 3: 138:86718

REFERENCE 4: 138:83723

REFERENCE 5: 138:69369

REFERENCE 6: 138:69322

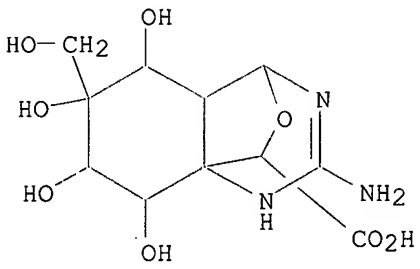
REFERENCE 7: 138:68171

REFERENCE 8: 138:68040

REFERENCE 9: 138:49952

REFERENCE 10: 138:38538

L60 ANSWER 8 OF 13 REGISTRY COPYRIGHT 2003 ACS
RN **3270-35-7** REGISTRY
CN 1H-4,8a-(Epoxymethano)quinazoline-9-carboxylic acid, 2-amino-4,4a,5,6,7,8-hexahydro-5,6,7,8-tetrahydroxy-6-(hydroxymethyl)-, (4S,4aR,5R,6S,7R,8R,8aR,9R)- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN 1H-4,8a-(Epoxymethano)quinazoline-9-carboxylic acid, 2-amino-4,4a,5,6,7,8-hexahydro-5,6,7,8-tetrahydroxy-6-(hydroxymethyl)-, [4S-(4.alpha.,4a.beta.,5.alpha.,6.beta.,7.beta.,8.beta.,8a.alpha.,9S*)]-
CN Tetrodonic acid (7CI, 8CI)
MF C11 H17 N3 O8
CI COM
LC STN Files: BEILSTEIN*, BIOBUSINESS, BIOSIS, CA, CAOLD, CAPLUS, MEDLINE, NAPRALERT, RTECS*, TOXCENTER, USPATFULL
(*File contains numerically searchable property data)



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

29 REFERENCES IN FILE CA (1962 TO DATE)
29 REFERENCES IN FILE CAPLUS (1962 TO DATE)
5 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

REFERENCE 1: 137:363099

REFERENCE 2: 137:304801

REFERENCE 3: 137:1763

REFERENCE 4: 136:406875

REFERENCE 5: 136:241691

REFERENCE 6: 136:226808

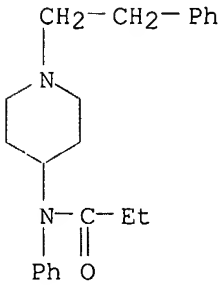
REFERENCE 7: 135:18727

REFERENCE 8: 133:359932

REFERENCE 9: 131:154655

REFERENCE 10: 128:303619

L60 ANSWER 9 OF 13 REGISTRY COPYRIGHT 2003 ACS
RN **437-38-7** REGISTRY
CN Propanamide, N-phenyl-N-[1-(2-phenylethyl)-4-piperidinyl]- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Propionanilide, N-(1-phenethyl-4-piperidyl)- (7CI, 8CI)
OTHER NAMES:
CN 1-Phenethyl-4-(N-phenylpropionamido)piperidine
CN 1-Phenethyl-4-N-propionylanilinopiperidine
CN Durogesic
CN Fentanest
CN Fentanil
CN Fentanyl
CN N-[1-(2-Phenylethyl)-4-piperidinyl]propionanilide
CN Phentanyl
CN R 4263
FS 3D CONCORD
DR 80832-90-2
MF C22 H28 N2 O
CI COM
LC STN Files: ADISINSIGHT, ADISNEWS, AGRICOLA, ANABSTR, BEILSTEIN*, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CABA, CANCERLIT, CAOLD, CAPLUS, CASREACT, CBNB, CEN, CHEMCATS, CHEMLIST, CIN, CSCHEM, CSNB, DDFU, DIOGENES, DRUGNL, DRUGU, DRUGUPDATES, EMBASE, HODOC*, HSDB*, IFICDB, IFIUDB, IPA, MEDLINE, MRCK*, MSDS-OHS, NIOSHTIC, PHAR, PHARMASEARCH, PROMT, RTECS*, SPECINFO, TOXCENTER, USAN, USPAT2, USPATFULL, VETU
(*File contains numerically searchable property data)
Other Sources: EINECS**, WHO
(**Enter CHEMLIST File for up-to-date regulatory information)



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

2763 REFERENCES IN FILE CA (1962 TO DATE)
80 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
2768 REFERENCES IN FILE CAPLUS (1962 TO DATE)
20 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

REFERENCE 1: 138:142483

REFERENCE 2: 138:142316

REFERENCE 3: 138:130907

REFERENCE 4: 138:130900

REFERENCE 5: 138:130394

REFERENCE 6: 138:127066

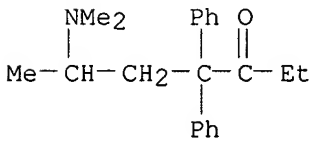
REFERENCE 7: 138:117582

REFERENCE 8: 138:117574

REFERENCE 9: 138:117555

REFERENCE 10: 138:112472

L60 ANSWER 10 OF 13 REGISTRY COPYRIGHT 2003 ACS
RN **76-99-3** REGISTRY
CN 3-Heptanone, 6-(dimethylamino)-4,4-diphenyl- (7CI, 8CI, 9CI) (CA INDEX NAME)
OTHER NAMES:
CN (.+-.)-Methadone
CN 6-Dimethylamino-4,4-diphenyl-3-heptanone
CN Algovetin
CN Amidone
CN Diaminon
CN dl-Methadone
CN Dolophin
CN Eptadone
CN Heptadone
CN Heptanon
CN Heptanon (pharmaceutical)
CN Metasedin
CN Methadone
CN Phenadone
CN Physeptone
CN Racemic methadone
CN Sedo-Rapide
FS 3D CONCORD
DR 297-88-1
MF C21 H27 N O
CI COM
LC STN Files: ADISNEWS, AGRICOLA, ANABSTR, BEILSTEIN*, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CABA, CANCERLIT, CAOLD, CAPLUS, CASREACT, CBNB, CEN, CHEMCATS, CHEMLIST, CIN, CSCHEM, DDFU, DIOGENES, DRUGU, EMBASE, HODOC*, HSDB*, IFICDB, IFIPAT, IFIUDB, IPA, MEDLINE, MRCK*, NIOSHTIC, PHARMASEARCH, PROMT, RTECS*, SPECINFO, TOXCENTER, USAN, USPAT2, USPATFULL, VETU
(*File contains numerically searchable property data)
Other Sources: EINECS**, WHO
(**Enter CHEMLIST File for up-to-date regulatory information)



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

2333 REFERENCES IN FILE CA (1962 TO DATE)
46 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
2338 REFERENCES IN FILE CAPLUS (1962 TO DATE)
1 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

REFERENCE 1: 138:118594

REFERENCE 2: 138:117520

REFERENCE 3: 138:112555

REFERENCE 4: 138:102127

REFERENCE 5: 138:102125

REFERENCE 6: 138:101312

REFERENCE 7: 138:100807

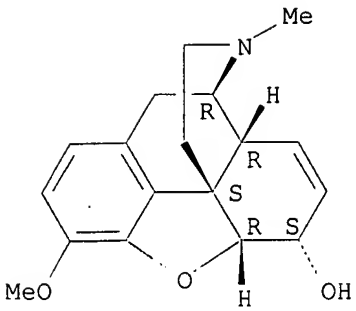
REFERENCE 8: 138:95716

REFERENCE 9: 138:84582

REFERENCE 10: 138:49798

L60 ANSWER 11 OF 13 REGISTRY COPYRIGHT 2003 ACS
RN **76-57-3** REGISTRY
CN Morphinan-6-ol, 7,8-didehydro-4,5-epoxy-3-methoxy-17-methyl-, (5.alpha.,6.alpha.)- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Morphinan-6.alpha.-ol, 7,8-didehydro-4,5.alpha.-epoxy-3-methoxy-17-methyl- (8CI)
OTHER NAMES:
CN (-)-Codeine
CN Codeine
CN Codicept
CN Coducept
CN l-Codeine
CN Methylmorphine
CN Morphine 3-methyl ether
CN Morphine monomethyl ether
CN O3-Methylmorphine
FS STEREOSEARCH
DR 120210-43-7, 79990-78-6
MF C18 H21 N O3
CI COM
LC STN Files: ADISNEWS, AGRICOLA, ANABSTR, BEILSTEIN*, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CABA, CANCERLIT, CAOLD, CAPLUS, CASREACT, CBNB, CEN, CHEMCATS, CHEMINFORMRX, CHEMLIST, CIN, CSCHEM, CSNB, DDFU, DETHERM*, DIOGENES, DRUGU, EMBASE, GMELIN*, HODOC*, HSDB*, IFICDB, IFIPAT, IFIUDB, MEDLINE, MRCK*, MSDS-OHS, NAPRALERT, NIOSHTIC, PHARMASEARCH, PROMT, RTECS*, SPECINFO, TOXCENTER, USAN, USPAT2, USPATFULL, VETU
(*File contains numerically searchable property data)
Other Sources: EINECS**
(**Enter CHEMLIST File for up-to-date regulatory information)

Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

4031 REFERENCES IN FILE CA (1962 TO DATE)
54 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
4040 REFERENCES IN FILE CAPLUS (1962 TO DATE)
1 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

REFERENCE 1: 138:142593

REFERENCE 2: 138:133514

REFERENCE 3: 138:132331

REFERENCE 4: 138:132330

REFERENCE 5: 138:132329

REFERENCE 6: 138:132323

REFERENCE 7: 138:132315

REFERENCE 8: 138:131153

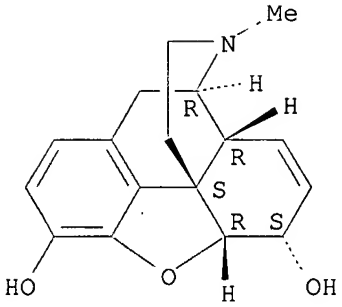
REFERENCE 9: 138:118594

REFERENCE 10: 138:117574

L60 ANSWER 12 OF 13 REGISTRY COPYRIGHT 2003 ACS
RN **57-27-2** REGISTRY
CN Morphinan-3,6-diol, 7,8-didehydro-4,5-epoxy-17-methyl-
(5.alpha.,6.alpha.)- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Morphinan-3,6.alpha.-diol, 7,8-didehydro-4,5.alpha.-epoxy-17-methyl- (8CI)
OTHER NAMES:
CN (-)-Morphine
CN Dulcontin
CN Duromorph
CN l-Morphine
CN Meconium
CN Morphia
CN Morphin
CN Morphina
CN Morphine
CN Morphinism
CN Morphinum
CN Morphium
CN MS Contin
CN Nepenthe

CN Ospalivina
FS STEREOSEARCH
DR 8053-16-5, 85201-37-2, 47106-99-0
MF C17 H19 N O3
CI COM
LC STN Files: ADISINSIGHT, ADISNEWS, AGRICOLA, ANABSTR, BEILSTEIN*, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CABA, CANCERLIT, CAPLUS, CASREACT, CBNB, CEN, CHEMCATS, CHEMINFORMRX, CHEMLIST, CIN, CSCHEM, CSNB, DDFU, DETHERM*, DIOGENES, DRUGU, EMBASE, GMELIN*, HODOC*, HSDB*, IFICDB, IFIPAT, IFIUDB, IPA, MEDLINE, MRCK*, MSDS-OHS, NAPRALERT, NIOSHTIC, PHAR, PHARMASEARCH, PIRA, PROMT, RTECS*, SPECINFO, TOXCENTER, USAN, USPAT2, USPATFULL, VETU
(*File contains numerically searchable property data)
Other Sources: EINECS**
(**Enter CHEMLIST File for up-to-date regulatory information)

Absolute stereochemistry. Rotation (-).



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

20056 REFERENCES IN FILE CA (1962 TO DATE)
241 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
20082 REFERENCES IN FILE CAPLUS (1962 TO DATE)

REFERENCE 1: 138:142593

REFERENCE 2: 138:142316

REFERENCE 3: 138:137023

REFERENCE 4: 138:133514

REFERENCE 5: 138:133007

REFERENCE 6: 138:132508

REFERENCE 7: 138:132330

REFERENCE 8: 138:132329

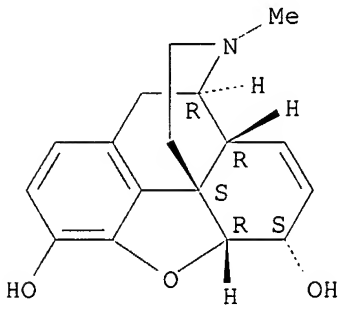
REFERENCE 9: 138:132328

REFERENCE 10: 138:132324

L60 ANSWER 13 OF 13 REGISTRY COPYRIGHT 2003 ACS
RN **52-26-6** REGISTRY
CN Morphinan-3,6-diol, 7,8-didehydro-4,5-epoxy-17-methyl-(5.alpha.,6.alpha.)-, hydrochloride (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:

CN Morphinan-3,6.alpha.-diol, 7,8-didehydro-4,5.alpha.-epoxy-17-methyl-, hydrochloride (8CI)
OTHER NAMES:
CN (-)-Morphine hydrochloride
CN Ampek
CN Epimore
CN Morphine chlorhydrate
CN Morphine hydrochloride
CN Theba-Intran
CN Thebametten
FS STEREOSEARCH
MF C17 H19 N O3 . Cl H
CI COM
LC STN Files: ADISINSIGHT, ANABSTR, BEILSTEIN*, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CAPLUS, CASREACT, CBNB, CHEMCATS, CHEMLIST, CIN, CSNB, DETHERM*, DIOGENES, EMBASE, GMELIN*, HSDB*, IPA, MRCK*, NIOSHTIC, PROMT, RTECS*, TOXCENTER, USAN, USPATFULL
(*File contains numerically searchable property data)
Other Sources: EINECS**
(**Enter CHEMLIST File for up-to-date regulatory information)
CRN (57-27-2)

Absolute stereochemistry. Rotation (-).



● HCl

1438 REFERENCES IN FILE CA (1962 TO DATE)
1 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
1438 REFERENCES IN FILE CAPLUS (1962 TO DATE)

REFERENCE 1: 138:130962

REFERENCE 2: 138:130903

REFERENCE 3: 138:100947

REFERENCE 4: 138:61304

REFERENCE 5: 138:49892

REFERENCE 6: 138:33188

REFERENCE 7: 138:29052

REFERENCE 8: 137:379912

REFERENCE 9: 137:363099

REFERENCE 10: 137:315958

=> fil wpix
FILE 'WPIX' ENTERED AT 10:28:13 ON 05 MAR 2003

FILE LAST UPDATED: 3 MAR 2003 <20030303/UP>
MOST RECENT DERWENT UPDATE: 200315 <200315/DW>
DERWENT WORLD PATENTS INDEX SUBSCRIBER FILE, COVERS 1963 TO DATE

>>> DUE TO TECHNICAL ISSUES THE SDIS FOR UPDATES 200302-200304
BASED ON ENTRY DATE (ED) MAY CONTAIN DOCUMENTS PREVIOUSLY
DISTRIBUTED. IF YOU ENCOUNTER ANY SURPLUS DOCUMENTS OF THIS
KIND, PLEASE CONTACT OUR HELPDESKS. UNJUSTIFIED CHARGES
INCURRED WILL BE REVOKED OF COURSE.
WE APOLOGIZE FOR ANY INCONVENIENCE CAUSED. <<<

>>> SLART (Simultaneous Left and Right Truncation) is now
available in the /ABEX field. An additional search field
/BIX is also provided which comprises both /BI and /ABEX <<<

>>> PATENT IMAGES AVAILABLE FOR PRINT AND DISPLAY <<<

>>> FOR DETAILS OF THE PATENTS COVERED IN CURRENT UPDATES,
SEE http://www.derwent.com/dwpi/updates/dwpicov/index.html <<<

>>> FOR A COPY OF THE DERWENT WORLD PATENTS INDEX STN USER GUIDE,
PLEASE VISIT:
http://www.stn-international.de/training_center/patents/stn_guide.pdf <<<

>>> FOR INFORMATION ON ALL DERWENT WORLD PATENTS INDEX USER
GUIDES, PLEASE VISIT:
http://www.derwent.com/userguides/dwpi_guide.html <<<

=> d all abeq tech abex tot

L123 ANSWER 1 OF 2 WPIX (C) 2003 THOMSON DERWENT
AN **2003-140323** [13] WPIX
DNC **C2003-035545**
TI New composition useful for producing analgesia in a mammal for treating e.g. chronic or acute pain, comprises an opioid e.g. **morphine**, a sodium channel blocker e.g. **tetrodotoxin**, and a carrier.
DC B05
IN KU, B; SHUM, F H K
PA (WEXM-N) WEX MEDICAL INSTR CO LTD
CYC 100
PI WO 2002094272 A1 20021128 (200313)* EN 18p A61K031-517
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZM ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ OM PH PL PT RO RU SD SE SG SI SK SL TJ TM TN TR TT TZ UA UG US UZ VN YU ZA ZM ZW
ADT WO 2002094272 A1 WO 2002-CN339 20020520
PRAI CN 2001-118098 20010518
IC ICM A61K031-517
ICS **A61K031-485**; A61P025-04

AB WO 200294272 A UPAB: 20030224
NOVELTY - New composition comprises:
(1) an opioid (a);
(2) a sodium channel blocker (b) that binds to the SS1 or SS2 subunit of a sodium channel; and
(3) a carrier (c).
ACTIVITY - Analgesic; Cytostatic; Osteopathic; Tranquilizer.
MECHANISM OF ACTION - Pain inhibitor; Sodium channel blocker; Opioid agonist.
A test was performed to evaluate pain inhibition. Wistar male rats with a body weight of 180-300 g were dosed intramuscularly. Normal saline was used as control, TTX (0.39 micro g/kg) co-administered with **morphine** (0.19 micro g/kg), in a volume of 0.1 ml/100 g body weight. The assay was performed according to the method described in Voges et al..
The medium inhibition dose, ID50 was determined and was found to be 66.2.
USE - For producing analgesia in a mammal (claimed) for treating chronic or acute pain, bone degenerative diseases and cancer. (a) can also be used to achieve a depressive effect on the central nervous system.
ADVANTAGE - Co-administering opioids (a) and sodium channel blocker (b) produces analgesia and results in a greater-than-additive effect.
Dwg.0/5
FS CPI
FA AB; DCN
MC CPI: B04-A04; B06-D17; B06-E05; B07-D05; B14-C01; B14-H01B; B14-J01B; B14-N01
TECH UPTX: 20030224
TECHNOLOGY FOCUS - ORGANIC CHEMISTRY - Preferred Components: The compound that binds to the SS1 or SS2 subunit of a sodium channel is **tetrodotoxin** (preferably octahydro-12-(hydroxymethyl)-2-imino-5,9:7,10a-dimethano-10aH-(1,3)dioxocino(6,5-d)pyrimidine-4,7,10,11,12-pentol) or its derivatives or **saxitoxin** (preferably 2,6-diamino-4-((aminocarbonyl)oxy)methyl-3a,4,8,9-tetrahydro-1H,10H-pyrrolo(1,2-c)purine-10,10-diol(3aS-(3a-a-a-4-a,10aRasterisk)) or its salts.
(b) is at least one selected from **tetrodotoxin** (TTX), **anhydrotetrodotoxin, tetrodaminotoxin, methoxytetrodotoxin, ethoxytetrodotoxin, deoxytetrodotoxin** or **tetrodonic acid**.
The **saxitoxin** comprises a tetrahydropurine moiety composed of two guanidine units fused together in a stable azaketal linkage, having a molecular formula C10H17N7O4.
Preferred Composition: The ratio of (b):(a) is 1:100-1:30000.
ABEX
SPECIFIC COMPOUNDS - **Morphine, codeine, methadone** and **fentanyl** are specifically claimed as (a).

ADMINISTRATION - The dosage of **tetrodotoxin** or **saxitoxin** is 0.01-20 microg/kg and the dosage of **morphine** is 0.002-20 mg/kg and administered separately. The administration is intrathecally or intramuscularly (all claimed).

EXAMPLE - No relevant example given.

L123 ANSWER 2 OF 2 WPIX (C) 2003 THOMSON DERWENT
AN **2002-434994** [46] WPIX
DNC **C2002-123478**
TI Production of analgesia in a mammal experiencing pain e.g. neuropathic pain, cancer pain involves systemic administration of a sodium channel blocking compound e.g. **tetrodotoxin** in a vehicle.
DC B02
IN DONG, Q; SHUM, F H K; SHUM, F H

PA (WEXM-N) WEX MEDICAL INSTR CO; (WEIK-N) WEIKESI MEDICAL INSTR CO LTD; (WEXM-N) WEX MEDICAL INSTR CO LTD

CYC 96

PI WO 2002022129 A1 20020321 (200246)* EN 60p A61K031-517
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW
US 6407088 B1 20020618 (200248) A61K031-33
AU 2002013785 A 20020326 (200251) A61K031-517
CN 1356104 A 20020703 (200265) A61K031-505

ADT WO 2002022129 A1 WO 2001-CN1391 20010911; US 6407088 B1 US 2000-695053 20001025; AU 2002013785 A AU 2002-13785 20010911; CN 1356104 A CN 2000-124517 20000918

FDT AU 2002013785 A Based on WO 200222129

PRAI CN 2000-124517 20000918

IC ICM A61K031-33; A61K031-505; A61K031-517
ICS A61K031-44; A61P023-02; A61P025-04

AB WO 200222129 A UPAB: 20020722

NOVELTY - Production of analgesia in a mammal experiencing pain involves systemic administration of a sodium channel blocking compound (I) in a vehicle.

DETAILED DESCRIPTION - An INDEPENDENT CLAIM is included for a kit comprising a composition (compound (I) and a carrier), and a written material describing systemic administration of the composition for the treatment of pain.

ACTIVITY - Analgesic.

Wister rats (180 - 240 g, half of each sex) were randomly divided into **tetrodotoxin** (TTX)-tested groups, positive control groups (aspirin or meperidine) and negative control group (normal saline (NS)). The mice were fasted for 12 hours before the test, and allowed to drink ad-libitum. TTX was given subcutaneously or intramuscularly and 40 minutes later, 0.6% acetic acid (0.1 ml/10 g) was given intraperitoneally as a chemical stimulus. The writhing incidence in the mice was observed and was recorded within the following 15 minutes. The mice in NS group, aspirin group and Meperidine groups were treated the same way. The writhing incidences in the TTX groups were compared to the control group and ID50 was calculated. The ID50 in the TTX, aspirin and meperidine treated mice was found to be: 2.68 micro g/kg, 198.8 mg/kg and 1.8 mg/kg, respectively. Thus the analgesic effect of TTX was much stronger than of aspirin and was 670 times stronger than meperidine. The analgesic potency of TTX was also found to be similar in different routes of administration.

MECHANISM OF ACTION - Sodium channel blocker.

USE - For producing analgesia in a mammal experiencing pain caused by mechanical, chemical, or ischemic stimulation, or inflammation, neuropathic pain, and pain arising from cancer such as liver, rectal, bone, lymphatic, esophageal, genital organs, prostate, digestive system, stomach, colon, breast, respiratory system, lung, bronchial, urinary, skin cancer, lymphoma, leimyosarcoma (all claimed), central pain, and phantom limb pain.

ADVANTAGE - The sodium channel blocking compound does not cause drug dependence or addiction in the mammal (preferably a female of childbearing age), does not have any non-reversible adverse effect, does not produce local intramuscular irritation at the region where the systemic administration is performed, does not produce any general hypersensitivity reaction in the mammal, and does not induce haemolyzation or vascular stimulation in the mammal (claimed).

The short course of treatment of **tetrodotoxin** of only 3 days, as compared to any other strong analgesics that must be administered consistently and continuously to be effective, and thus exhibits considerable advantages over any other of the currently used analgesics.

After administration of the **tetrodotoxin** after 3 days, the analgesic effect lasts for 20 - 30 days. **Tetrodotoxin** also produced evident detoxification in the patients who were dependent on dolantin.
Dwg.0/0

FS CPI
FA AB; DCN
MC CPI: B06-D17; B06-E05; B14-C01; B14-L06
TECH UPTX: 20020722

TECHNOLOGY FOCUS - PHARMACEUTICALS - Preferred Composition: The composition comprises an acetic acid solution of **tetrodotoxin** when the administration is by injection.
Preferred Compound: (I) has a tetrahydropurine moiety comprising two guanidine units fused together in a stable azaketal linkage, having a molecular formula C10H17N7O4, (molecular weight = 299.30), or its derivative.

ABEX

SPECIFIC COMPOUNDS - **Tetrodotoxin, anhydrotetrodotoxin, tetrodaminotoxin, methoxytetrodotoxin**, ethoxy-**tetrodotoxin, deoxytetrodotoxin, tetrodonic acid**, hydroxysaxitoxin, and neosaxitoxin are specifically claimed as (a).

ADMINISTRATION - (I) is administered systematically (by intramuscular injection, subcutaneous injection, intravenous injection), orally, sublingually, skin patch, implantable osmotic pump, collagen implant, aerosol inhalation, or suppository. The dosage is (0.1 - 5) mug/kg body weight at least once (preferably every 3 - 12 hours during a treatment period of 1 - 10 (preferably 3) days) in a repeated treatment (claimed).

EXAMPLE - A 44 year old male had developed abdominal pain and was diagnosed with smooth muscle pain in the back wall of his celiac for which he underwent a surgical procedure. One year later, his abdomen pain relapsed and he was operated on again. The pathological examination from the second operation revealed that he had developed a smooth muscle sarcoma (leiomyosarcoma), later finding that his sarcoma had spread to his liver and that he now required and received anti-cancer treatment (chemotherapy). He began to inject dolantin (control) due to the severe pain in his abdomen. He needed to inject dolantin at least 3 times per day. Initially he was taking the dolantin by intramuscular injection, and finally he needed to use intravenous injection in order to have the dolantin take effect faster. Just prior to when he received the **tetrodotoxin** (test) treatment, he had taken over 100 injections of dolantin in the previous month. At the beginning, when he stopped using dolantin, he experienced **morphine**-like withdrawal symptoms, such as whole body weakness and pain, trembling when standing up and difficulty walking. He voluntarily received **tetrodotoxin** treatment. His pain intensity was severe before using **tetrodotoxin**. 5 minutes after the first injection of **tetrodotoxin**, the pain was completely disappeared. After 3 days of treatment, the patient was able to live normally and continue to feel comfortable without any pain.

=> d his

(FILE 'HOME' ENTERED AT 09:22:31 ON 05 MAR 2003)
SET COST OFF

FILE 'REGISTRY' ENTERED AT 09:22:41 ON 05 MAR 2003
L1 4 S (MORPHINE OR CODEINE OR METHADONE OR FENTANYL)/CN
L2 7 S (SAXITOXIN OR TETRODONIC ACID OR ETHOXYTETRODOTOXIN OR TETROD
E TTRODIAMINOTOXIN
E TDTRODIAMINOTOXIN

```
                E TETRODIAMINOTOXIN
                E TETRADIAMINOTOXIN

     FILE 'HCAPLUS' ENTERED AT 09:24:41 ON 05 MAR 2003
L3        25258 S L1
L4        43711 S MORPHINE OR CODEINE OR METHADONE OR METADONE OR FENTANYL
L5        44759 S L3,L4
L6         2764 S L2
L7        11980 S SAXITOXIN OR TETRODONIC ACID OR ETHOXYTETRODOTOXIN OR TETRODO
L8            0 S ?TETRODIAMINOTOXIN?
L9            0 S ?DIAMINOTOXIN?
L10           0 S ?DIAMINODOTOXIN?
L11         190 S L5 AND L6,L7
L12           1 S L11 AND (SS1 OR SS2)

     FILE 'REGISTRY' ENTERED AT 09:27:03 ON 05 MAR 2003
L13           1 S 7724-38-1

     FILE 'HCAPLUS' ENTERED AT 09:27:17 ON 05 MAR 2003
L14          16 S L13
L15           0 S TETRODIAMINOTOXIN
L16          14 S TETRODAMINOTOXIN
L17           1 S L14,L15 AND L5
L18           1 S L12,L17
L19           1 S L18 AND L3-L12,L14-L18

     FILE 'REGISTRY' ENTERED AT 09:28:16 ON 05 MAR 2003
                SEL RN L1
L20         432 S E1-E4/CRN
L21           8 S L2,L13
                SEL RN
L22          85 S E5-E12/CRN
L23           0 S L20 AND L22

     FILE 'HCAPLUS' ENTERED AT 09:28:41 ON 05 MAR 2003
L24        5564 S L20
L25       45130 S L5,L24
L26          55 S L22
L27       12078 S L6,L7,L14,L16,L26
L28         191 S L25 AND L27
L29           1 S L28 AND (SS1 OR SS2)
                E ION CHANNEL/CT
                E E34
L30        1559 S E3
                E ION CHANNEL/CT
                E E27+ALL
L31         893 S E4 (L) SODIUM
L32          75 S E4 (L) (SS1 OR SS2 OR SUBTYP? OR SUBUNIT?)
L33           0 S L28 AND L30
L34           2 S L28 AND L31
L35           0 S L28 AND L32
L36         125 S L28 AND (SYNERG? OR MIX? OR FORMUL? OR COMBIN? OR COMPOSITION
L37          11 S L36 AND (NA OR SODIUM)(L)CHANNEL?
L38          40 S L3,L24 AND L6,L14,L26
L39          40 S L38 AND L28-L37
L40          94 S L36 NOT L37-L39
L41           3 S L40 AND (OPPOSITE OR ATTENUAT?)/TI
L42          49 S L28 NOT L36-L41
                E KU B/AU
L43          45 S E3-E9
                E SHUM F/AU
L44           9 S E3,E8,E10
                E KONG F/AU
```

```
                E KONG FRANK/AU
                E KONG S/AU
                E KONG SHUM/AU
L45           6 S L43,L44 AND L25-L27
L46          32 S (SHUM H? OR SHUM F?)/AU
L47           7 S L46 AND L25-L27
L48           8 S L45;L47
L49           5 S L48 NOT (EXTRACT? OR PURIF?)/TI
L50           6 S L34,L49 AND L3-L12,L14-L19,L24-L49
L51       14352 S L27 OR L30 OR L31 OR L32
L52        8935 S (NA OR SODIUM)(L)CHANNEL?(L)BLOCK?
L53          52 S L52 AND L25
L54         119 S L52 AND (NARCOTIC OR OPIOID OR OPIATE)
L55         142 S L53,L54
L56         128 S L55 NOT L36-L42,L11
L57          48 S L56 AND ION CHANNEL?/CT
                SEL DN AN 9 42
L58           2 S E1-E6
L59           8 S L50,L58 AND L3-L12,L14-L19,L24-L58
                SEL HIT RN

    FILE 'REGISTRY' ENTERED AT 09:53:22 ON 05 MAR 2003
L60          13 S E7-E19

    FILE 'HCAPLUS' ENTERED AT 09:53:57 ON 05 MAR 2003

    FILE 'REGISTRY' ENTERED AT 09:54:14 ON 05 MAR 2003

    FILE 'EMBASE' ENTERED AT 09:54:28 ON 05 MAR 2003
L61       69876 S L1
L62       55692 S L20
L63       69876 S (MORPHINE OR CODEINE OR METHADONE OR FENTANYL)/CT
                E OPIOID/CT
                E E3+ALL
                E E2+ALL
L64       18143 S E1+NT
                E NARCOTIC/CT
                E E7+ALL
L65      102041 S E4+NT
L66      110189 S L61-L65
L67       13460 S L21 OR L22
L68       16054 S L7 OR L16
L69       16054 S L67,L68
                E SODIUM CHANNEL/CT
                E E4+ALL
L70        3133 S E4+NT
L71        1958 S E7+NT
L72         474 S L66 AND L69
L73         117 S L66 AND L70
L74         182 S L66 AND L71
L75         659 S L72-L74
                E DRUG SYNERG/CT
                E E4+ALL
                E E2+ALL
L76          18 S E1+NT AND L75
L77        8338 S L66 (L) CB/CT
L78          29 S L77 AND L75
L79         192 S L69-L71 (L) CB/CT
L80          16 S L79 AND L75
L81          33 S L78,L80
L82           6 S L81 NOT AB/FA
L83          27 S L81 NOT L82
```

```
     FILE 'CANCERLIT' ENTERED AT 10:15:43 ON 05 MAR 2003
L84         2284 S L1 OR L20
L85         3492 S L4
L86         3492 S L84-L85
L87          276 S L21 OR L22
L88          452 S L7 OR L16
L89          452 S L87,L88
L90            2 S L86 AND L89

     FILE 'MEDLINE' ENTERED AT 10:17:00 ON 05 MAR 2003
L91        50827 S L86
L92        14592 S L89
L93          180 S L91 AND L92
L94           38 S L93 NOT AB/FA
                 E SYNERG/CT
                 E E6+ALL
                 E E2+ALL
L95        40145 S E4+NT
                 E E3+ALL
                 E DRUG COMBINATION/CT
L96        34928 S E6+NT
                 E DRUG THERAPY, COMBINED/CT
                 E DRUG THERAPY, COMBINATION/CT
L97        72221 S E3+NT
L98            9 S L93 AND L95-L97

     FILE 'WPIX' ENTERED AT 10:20:48 ON 05 MAR 2003
L99         2313 S L4/BIX
                 E MORPHINE/DCN
                 E E3+ALL
L100         668 S E2 OR 0127/DRN
L101         214 S E4
L102           2 S E6
L103          39 S E8
L104          81 S E14
                 E CODEINE/DCN
                 E E3+ALL
L105         374 S E2 OR 0405/DRN
L106         137 S E4
L107          48 S E8
L108          11 S E10
                 E METHADONE/DCN
                 E E3+ALL
L109         185 S E2 OR 0408/DRN
L110           6 S E4
                 E FENTANYL/DCN
                 E E3+ALL
L111         252 S E2 OR 1254/DRN
L112         128 S E4
L113          20 S E6
L114        2645 S L99-L113
L115          75 S L7/BIX OR L16/BIX
                 E SAXITOXIN/DCN
                 E E3+ALL
L116          17 S E2
                 E TETRODONIC ACID/DCN
                 E ETHOXYTETRODOTOXIN/DCN
                 E TETRODOTOXIN/DCN
                 E E3+ALL
L117          19 S E2
                 E ANHYDROTETRODOTOXIN/DCN
                 E TETRODAMINOTOXIN/DCN
                 E METHOXYTETRODOTOXIN/DCN
```

```
                E DEOXYTETRODOTOXIN/DCN
L118           80 S L115-L117
L119            4 S L114 AND L118
                SEL DN AN 1 2
L120            2 S L119 AND E1-E4
L121          660 S A61K031-485/IC,ICM,ICS,ICA,ICI
L122            1 S L121 AND L118
L123            2 S L120,L122

     FILE 'WPIX' ENTERED AT 10:28:13 ON 05 MAR 2003

     FILE 'DPCI' ENTERED AT 10:28:34 ON 05 MAR 2003
                E WO2002094272/PN
```